2009

PREDICTING SHORT INTERPREGNANCY INTERVALS IN WOMEN FROM UNDERSERVED POPULATIONS IN LONDON, ONTARIO

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Spine title: Predicting Short Interpregnancy Intervals

Thesis format: Monograph

by

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Graduate Program in Population Epidemiology

A thesis submitted in partial fulfillment
of the requirements for the degree of
Master of Science

The School of Graduate and Postdoctoral Studies
The University of Western Ontario
London, Ontario, Canada

Abstract

Background: Becoming pregnant within 6 months of previous birth is strongly associated with several adverse perinatal and maternal outcomes.

Purpose: To develop a model that can predict which women are at greatest risk of experiencing a short interpregnancy interval (IPI).

Methods: Retrospective case-control design was employed using potential predictors collected from medical records. Logistic regression was used to develop a multivarible predictive model identifying key risk factors.

Results: Patients were at greatest risk of experiencing a short IPI if they held refugee status (OR: 10.56; 95% CI: 1.36, 81.70), were in a common law relationship (OR: 7.16; 95% CI 1.43, 44.81), had no specified occupation (OR: 1.30; 95% CI: 1.10, 1.94), or had the Children's Aid Society involved in the care of index children (OR: 4.93; 95% CI: 1.28, 18.72). To maximize utility, a predictive nomogram was constructed.

Conclusions: Results can be used to prompt preventative care.

Keywords: maternal health, interpregnancy interval, birth spacing, underserved populations, community health, logistic regression, predictive nomogram.

Acknowledgements

First, I would like to thank Dr. Greta Bauer for her support, advice and inspiration, and for trusting me enough to give me the freedom to make this project – with all its faults – truly my own. To Dr. G.Y. Zou for his patience in allowing me to tap into the vastness of his expertise in the face of my own inexperience. To Dr. William Avison for encouraging me to keep this project simple, clear and human.

There is no way to imagine the completion of this project without the support of Joanne Veldhorst, who expressed a special kind of empathy that is so rare in a clinical advisor. I have utmost appreciation for Lucy and the reception staff at the London Intercommunity Health Centre for graciously accepting the burden that I was, and to the nursing and support staff who made data collection enjoyable. Thank-you to Jennifer Rayner for answering a thousand questions along the way.

This project could not have been completed without the help of Stephanie Dixon, who showed me what it means to truly love what you do (even if that involves R), and Pat Prendergast, whose experiences were easy to cling to. Thank-you to Todd Coleman, Shamara Baidoobonso, Nooshin Khobzi and the rest of the 'Infection and Equity Group' for their support and critical eye.

Gratitude and apologies to my family, Bob, Joanne, Kristin and Katie Hohenadel, Joe Frank, and all of the Weadicks and Hohenadels, for being the ultimate support system. To my friends in London, especially Wyatt Smith, Shannon Clutton, Megan McKeown, Todd Coleman (again), and Katie Bradley for doing whatever was necessary to me get through: an ear, a distraction, or a free pass. Thank-you to my friends in Guelph, Toronto, Buffalo, Weymouth, and elsewhere for allowing me to "go underground." Finally, to Brie Yama, for being the ultimate cheerleader, editor, and fast friend.

Dedication

This thesis is dedicated to the women of the London Intercommunity Health Centre's prenatal clinic. Your stories moved me in ways that rarely occur when conducting quantitative research.

And to Teresa Weadick, whose passing made this thesis difficult to write at times, but whose life reminded me that hard work is always worthwhile.

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1 CHAPTER ONE: INTRODUCTION

This project was undertaken with the expectation that the results would enhance the capacity of the London Intercommunity Health Centre (LIHC) in London, Ontario, Canada to provide preventative care to clients from underserved populations. This is important because the LIHC aims to "support individuals and families whose poverty, isolation, age, lack of housing or recent immigration prevent access to services."[1]

This project began with a discussion between the student-researcher and LIHC clinicians to identify areas of interest and research products that would be useful in clinical practice. Following this discussion, the literature was consulted to establish the importance of identified issues in the greater population. As a result of this process, the specific goal of this project became to develop a model that can predict which women using the LIHC prenatal program are at greatest risk of experiencing a short interpregnancy interval. Such pregnancy occurs when conception takes place within 6 months of previous birth, and is also referred to as a short birth-to-conception interval.

Short interpregnancy intervals are the focus of inquiry for three reasons. First, clinicians at the LIHC prenatal clinic identified birth spacing as an important concern in their practice; second, there is reason to believe that women from underserved populations are more likely to conceive shortly after birth;[2] and third, there is well-established risk to mothers and infants in the greater population.[3,4]

Numerous studies have found that infants born to women with interpregnancy intervals 6 months or shorter had a significantly increased risk of preterm birth, low birth weight, and small for gestational age, compared to infants born to women with intervals of 18 to 23 months. Some studies also found links between short interpregnancy intervals and neonatal mortality and

morbidity.[3] Further, it has been shown that short interpregnancy intervals are associated with increased risks of placental abruption and placenta previa, and uterine rupture in women attempting a vaginal birth after previous cesarean delivery.[4]

Although there is a vast body of literature on the effects of interpregnancy intervals on infant and maternal health, few studies have attempted to develop a predictive model to determine which women are most likely experience short interpregnancy intervals, and no studies that were identified developed a clinical tool to predict women at risk.

The ability to predict short interpregnancy intervals may improve the health status of women attending the LIHC prenatal program and elsewhere by prompting increased preventative care, including special attention to nutritional depletion, a hypothesized cause of negative health outcomes resulting from short interpregnancy intervals.[3] Though an unexpectedly small sample size was obtained, the analysis of this work was conducted as carefully as possible in order to ensure the clinic received a useful tool. In the future, a larger scale study could be conducted to validate this tool and apply this model in other populations.

2 CHAPTER TWO: BACKGROUND

2.1 Background

Though there is a comprehensive body of literature on negative health outcomes associated with short interpregnancy intervals, there is very little information available on why women conceive shortly after birth. As a result, explanations of why short interpregnancy intervals occur will be examined speculatively through the examination of birth trends in Canada, patterns in birth spacing, fertility after birth, access to and use of contraceptive measures, and intention. Preceding a comprehensive look at the associated negative health outcomes, the causal mechanisms associated with this relationship will be explored, acknowledging that this is also a body of literature that is underdeveloped.

2.1.1 Birth Trends in Canada

Canadian fertility rates have declined substantially in the past fifty years, from an average of 3.9 births per woman in 1959[5] to an average of 1.59 births per woman in 2006.[6] There are a variety of explanations for this decline, including increased access to contraception, increased female participation in the workforce, higher educational attainment, postponement of marriage and first birth,[7] and changes in the structure of families and households including increased divorce rates, levels of unmarried cohabitation, number of blended and same-sex relationships, and the number of single parent households.[8]

Since 1986, the average age of first birth has risen from 27.0 to 29.3.[6] This increase in average age has both positive and negative consequences for mothers and their offspring. Women who experience first birth in their early to mid-twenties enjoy advantages associated with giving birth during their biological prime, but are at greater risk of experiencing poverty.[8]

Women who delay first birth are more likely to have attained higher education, established careers, and as a result possess greater financial security.[8] According to Tudiver, delayed child bearing is "a trend that can carry physical health disadvantages [but] may also carry social and economic advantages that, in turn, translate info benefits for healthy child development."[8]

2.1.1.1 Birth Spacing in Canada

Though Statistics Canada produces a variety of measures on fertility rates, place and mode of birth, birth outcome, and other pregnancy-related factors, information on birth spacing is sparse.[5] The most recent Canadian survey examining the timing and spacing of Canadian births was the Family History Survey (FHS), which was based on the sampling frame of the Canadian Labour Force Survey in 1984.[5]

The FHS measured 'birth interval,' referring to the time between two successive births, among 14,000 Canadian women. Results showed that there is a 2% chance of having a second birth within 12 months of the first, which loosely corresponds to a 3-month interpregnancy interval. There is a 28% chance of having a second birth within 24 months, a 56% chance within 36 months and an 84% chance within 72 months.[5] Patterns in spacing between second and third births follow similarly, if a third birth is to occur, with probability of 1% that a third birth will take place within 12 months of the second.[5]

There is reason to believe that women from underserved populations may be more likely to conceive shortly after previous birth, though this has not been explored in depth. Gold et al. conducted a study of birth spacing and income inequality in Washington State and found that the hazard of next birth from index birth was 309% greater for women in the most unequal counties compared to those in the most equal counties, suggesting that community-level income inequality may impact birth spacing.[2]

2.1.2 Why Short Interpregnancy Intervals Occur

The occurrence of short interpregnancy intervals is necessarily dependent on sexual activity, fertility, and patterns of contraception use after birth.

2.1.2.1 Sexual Activity After Birth

The resumption of sexual activity most often occurs within the first several months after birth. A study of 570 women and 550 of their partners in midwestern United States found that 17% of women had engaged in sexual intercourse at least once within 1 month of birth, 89% within 4 months, and 92% within 12 months.[10] There are several reasons for delayed resumption of sexual activity after birth. The first is related to residual pain and tenderness, caused by inadequate healing, episiotomy, residual bleeding, and inadequate lubrication due to decreases in estrogen production after birth. The second is simply fatigue.[10]

Women also tend to experience decreased sexual desire for several months after birth. This effects not only the resumption of sexual activity, but also the amount of sexual activity women engage in. Recent research indicates that 60% of women are having less sexual intercourse 5 months after birth than they were pre-pregnancy,[11] and more than 10% had not resumed their pre-pregnancy levels of sexual activity by 6 months post-partum.[12] These findings are contrary to previous research on sexual activity after birth, which indicated that interest in sexual activity returned to pre-pregnancy levels by four weeks post-delivery for most women.[11]

2.1.2.2 Fertility After Birth

The resumption of sexual activity after birth generally occurs concurrently with the reinstatement of a woman's fertility, depending on breastfeeding status. In mothers who bottle feed, or mix bottle and breastfeeding, first menstruation occurs at 8 weeks post-partum on

average, and 32 weeks post-partum in women who exclusively breastfeed. First ovulation occurs at approximately 10 weeks in women who bottle feed, or bottle and breastfeed, and 36 weeks in women who exclusively breastfeed.[13]

No published literature was found on the probability of conception without contraception during the first months after ovulation resumes post-partum. As a reference, in the general Canadian population, the Royal Commission for New Reproductive Technologies (RCNRT) estimates that 91.5% of women will conceive after regular sexual activity without contraception within one year, and 93% within two years.[14] It follows logically that an important factor in the occurrence or avoidance of a short inter-pregnancy interval must be related to contraceptive practices including breastfeeding, and access to, or the decision to use, other methods.

Breastfeeding

Many women - intentionally or unintentionally - use breastfeeding as a form of contraception during the months immediately after childbirth, as lactation inhibits ovulation by preventing estrogen secretion.[15] The effectiveness of this method relies on several factors. First, 4 hours or less must elapse between feedings during the day, and 6 hours or less during the night; second, the infant must be breastfed exclusively, without supplementation of solid foods or formula beyond 5-10% of their total nutritional intake.[15] If these conditions are met, breastfeeding is approximately 98% effective, which is analogous to oral contraceptive use.[15] It is likely that breastfeeding plays a substantial role in delaying conception after birth, as over two thirds of Canadian women initiate breastfeeding, though only 33% continue for more than 3 months.[16]

Contraceptive Use

Outside of the use of exclusive breastfeeding as a contraceptive measure, it is unclear how many women discuss the initiation of other forms of contraception after birth, or when this generally occurs. But, studies have shown that most women feel they are not getting the family planning support they need. Results from demographic and health surveys from 27 developing countries revealed that 60% of women believe their post-partum contraceptive needs have gone unmet.[17]

In a survey of new mothers conducted in the United Kingdom (n=174), less than 10% of the sample received any contraceptive information from their health care provider in hospital, and only 1.2% of women had a discussion with their general practitioner regarding post-natal contraception that could be described as "lengthy and helpful."[18] Most women received contraceptive information during their 6-week check-up, which is two weeks after the recommended start date for contraceptive protection.[18]

Access to and use of post-natal contraception not equal across populations. There is strong evidence that some women are less likely to initiate and maintain contraceptive use, and are more likely to engage in 'contraceptive risk taking.' Contraceptive risk taking is described as "the non-use of contraception by women who are sexually active, fertile, and not pregnant or trying to become pregnant."[19]

A study of demographic predictors of contraceptive risk taking using United States census data found that the women at highest risk were most likely to be Black or Hispanic (OR: 3.82; 95% CI: 1.60, 9.11), 30 years of age or younger (OR: 2.57; 95% CI: 1.23, 5.36), have beliefs about their reproductive cycle that are incorrect (OR: 2.51; 95% CI: 1.21, 5.19), and have previous children (OR: 3.21; 95% CI: 1.51, 6.82).[19] Though it is likely that a proportion of

pregnancies that occur shortly after birth can be attributed to a lack of access to, or understanding of, contraceptive measures, it is unclear how many occur by choice.

2.1.2.3 Intention

There is no published literature on why women choose to conceive shortly after childbirth. Some women experiencing short interpregnancy intervals may be doing so out of preference, for example, because they started to reproduce later in their childbearing years and would like to have more than one child,[7] or because they have religious, moral, or ideological oppositions to contraceptive use.[20,21] But, it is likely that many women experiencing a short interpregnancy interval do so unintentionally.

According to Statistics Canada, 39% of Canadian pregnancies are unintended.[22] Though rates of unintended pregnancies in Canada and the United States differ by 10%, with American rates of unplanned pregnancy at 49%, characteristics of women having this experience may be similar and thus will be explored in the absence of comparable Canadian data. It should be noted that 'intention' is difficult to measure in this context, and was measured by the pregnancy ending in terminating abortion, or occurring to a woman who identified herself as not wanting to be pregnant at that time or not intending to have any more children.

Analyses using three cycles of the American National Survey of Family Growth (NSFG) reveal that 48% of women experiencing an unintended pregnancy in the United States were using some form of contraception during the month of conception.[23] The highest proportion of unintended pregnancies occurred among the youngest cohort analyzed, with 83% of pregnancies in woman 18 and younger classified as unintended. The proportion of unintended pregnancies dropped to its lowest level (33%) in women in their early to mid thirties, and subsequently rose again among women aged 40 and older, reaching 51%.

Marital status plays an important role in rates of unintended pregnancies. Proportions were highest in women who had never been married, with 78% of pregnancies identified as unintended. Sixty three percent of pregnancies experienced by women who were formerly married were unintentional, compared to 31% of pregnancies experienced by married women.[23] The proportion of unintended pregnancies also varied greatly by poverty status. Women in poverty were far more likely to experience an unintended pregnancy, and the overall pregnancy rate declined with increasing income.[23]

2.1.3 Causal Mechanisms

Several theories have been put forward to explain the link between short interpregnancy intervals and negative health outcomes in infants and mothers, though few have been empirically tested. Largely, authors tend to favour explanations relating to maternal nutritional depletion and reject explanations based on socio-economic or lifestyle factors.

2.1.3.1 Socioeconomic Status and Lifestyle Factors

Critics of research conducted on interpregnancy intervals often raise the possibility that the relationship between short interpregnancy intervals and negative health outcomes could be explained by confounding.[24] To explain, several authors believe that short interpregnancy intervals are merely a marker for underlying risk factors, such as maternal socioeconomic status and lifestyle characteristics, which are established sources of risk for negative health outcomes for mothers and infants as opposed to there being a direct link between short interpregnancy intervals and a variety of maternal and infant health outcomes.[24,25]

This theory of association has been widely tested and disproved in a series of studies that aptly control for maternal socioeconomic status and lifestyle characteristics including a variety of

measures of socioeconomic status, instability, smoking, access to and proper use of health care services, unplanned pregnancies, and other behavioural or psychological determinants.[3,4] The association between short interpregnancy intervals and negative health outcomes is only marginally reduced after controlling for socioeconomic status and lifestyle factors such as smoking,[25,26] and differences do not persist between groups when analyses are conducted among samples stratified for socioeconomic, behavioural, and reproductive risk factors.[27] In addition, after controlling for outcomes of previous pregnancy, the association still does not appear to change, implying that short interpregnancy intervals are not just a marker of prior maternal risk.[26]

2.1.3.2 Biological Explanations

In addition to social and behavioural explanations, several biological explanations have been proposed to account for the link between negative maternal and infant health outcomes and short interpregnancy intervals, including preovulatory aging, maternal stress, and maternal nutritional depletion. Though there is no direct consensus in the field,[26] the former explanations are generally discarded in favour of the latter. Before discussing the role of nutritional depletion, several other proposed explanations will be explored, most of which are poorly supported or have not been studied rigorously.[26]

Preovulatory Overripeness

Though not directly tested using human subjects, pre- and postovulatory overripeness, a condition caused by delayed ovulation, has been associated with maldevelopment in laboratory animals, mainly amphibians.[28] Consequences of developmental issues tend to spring from gonad

malformations in the fetus.[28] This theory is highly underdeveloped and virtually untested in the literature.

Maternal Stress

Maternal stress has been connected with the risk of fetal death and preterm birth in various settings. Khoshnood et al. suggest that the connection between short interpregnancy intervals and adverse health outcomes may be due to the additional stress placed on a mother when becoming pregnant while caring for a young infant.[29]

Incomplete Healing of Uterine Scar

A possible explanation of the link between short interpregnancy intervals and uterine rupture in woman whose index birth was by cesarean section is that an insufficient amount of time has elapsed to allow for adequate healing of the uterine scar caused by incision. In a study using magnetic resonance imaging (MRI), Dicle et al. found that complete healing of uterine anatomy after cesarean section takes between six and nine months.[4]

Maternal Depletion Syndrome

The most supported causal explanation for the link between short interpregnancy intervals and negative health outcomes is related to Maternal Depletion Syndrome. According to Winkvist et al., Maternal Depletion Syndrome can be defined as "a negative change in maternal nutritional status during a reproductive cycle going from non-pregnant, non-lactating; to pregnancy; to lactation; to partial lactation; and back to non-pregnant nonlactating."[27] For some micronutrients affected by the reproductive cycle, such as vitamins A, B_6 and B_{12}, there is no reason to believe that fluctuating levels affect maternal and infant health due to short

interpregnancy intervals. Other factors such as iron, zinc and, most importantly, folate, may play highly important causal roles.[26,27]

Iron

Iron levels, like several other micronutrients, do not return to pre-pregnancy levels until several months after delivery. This is a possible explanatory factor because of the connection between iron deficiency in early pregnancy, preterm birth, and, consequently, low birth weight.[26] Though inadequate iron stores may be causally related to preterm birth and low birth weight, there is no reason to believe this deficiency is related to any other negative health outcomes associated with short interpregnancy intervals.[26]

Zinc

Though there is no published literature in support of this hypothesis to date, it is possible that low plasma zinc concentrations may also play a causal role in the link between short interpregnancy intervals, and preterm birth and low birth weight. The link between plasma zinc levels and preterm birth are readily established in the literature, and may be expanded to include cases where zinc levels are influenced by birth spacing.[27]

Folate

The most well-established micronutrient deficiency associated with negative health outcomes among women experiencing short interpregnancy intervals and their offspring is folate (vitamin B_9).[30] Folate is crucial in both pregnancy and lactation, as it aids cell division and growth through nucleic acid synthesis in the placenta and fetus.[31] It plays a crucial role in maternal health by increasing red cell mass, enlarging the uterus and placenta,[31] and aiding in the

production and secretion of breast milk.[27] Demand for folate is highest during gestational periods of rapid tissue growth.[31]

As a result, folate levels often do not recover for several months after birth. Smits and Essed found that one third of mothers had insufficient folate levels by the second to third month after delivery, and one fifth of mothers were still folate deficient by six months post partum.[26] Similarly, Bruinse and van den Berg assert that the "net cost of folacin during pregnancy is considerable, and repletion of folacin stores takes more than six months."[32]

Unlike other potential causal explanations for the link between negative health outcomes and short interpregnancy intervals, the effects of folate depletion have been tested independently. Folate depletion has been linked to several adverse health outcomes such as preterm delivery, low infant birth weight, fetal growth retardation, placental abruption and preeclampsia.[31,33]

In a study of 3,153 multiparous woman, van Eijsden found that each increase in interpregnancy interval between 1 and 24 months was significantly associated with a 63.1 gram increase in birth weight (95% CI: 42.8, 83.4). Further, they found that this effect could be mitigated by folic acid supplementation. Those who did not use folic acid supplementation experienced a statistically significant 165.3 gram decrease in birthweight (95% CI: 125.7, 204.9); those who started folate supplementation late experienced a statistically significant 33.5 gram decrease in birthweight (95% CI: -2.1, 69.1); and a non-significant decrease of 5.9 grams for early use (95% CI: -27.7, 39.5).[25] These results have two important implications: they add support for previous research that has suggested there is a negative association between short interpregnancy intervals and fetal growth, and they lend support for fetal depletion as a possible causal factor.[25]

It is likely that women from underserved populations are at a greater risk of experiencing the negative health outcomes associated with nutritional depletion because of pre-pregnancy dietary deficiencies and a lack of access to supplements.[31] The extent of folate depletion is dependent on the mother's pre-pregnancy levels, dietary intake and supplementation, and their ability to absorb the micronutrient. In non-pregnant women there are several genetic abnormalities that can lead to insufficient folate absorption, but most folate deficiencies are caused by inadequate dietary intake or supplementation, which are the only sources of folate for humans.[31]

It follows, as explained by Smits and Essed, that if a sufficient restoration has passed between birth and subsequent pregnancy, the mother's risk of folate deficiency will be the same in each subsequent pregnancy as the last. If there has not been a sufficient restoration period, the mother's risk of deficiency will be far higher and the recovery period longer.[26] This may explain why a minor increase in risk persists after controlling for socioeconomic and behavioural factors in outcome-based studies.

2.1.4 Associated Negative Health Outcomes

Despite the dearth of literature published on why short interpregnancy intervals occur, and the causal mechanisms that explain their effect, health outcomes related to closely spaced pregnancies for mothers and their offspring are well documented. It is worth reemphasizing that several authors have suggested that the link between negative health outcomes and short interpregnancy intervals is due to confounding, as women experiencing short interpregnancy intervals may be at greater reproductive risk independent of birth interval because of socioeconomic, behavioural, and lifestyle factors.[24] However, recent research on interpregnancy

intervals has been meticulous in controlling for these factors and results have not been significantly attenuated as a result.[3] Several strong associations persist for infants and mothers.

2.1.4.1 Infant Health

Preterm Birth

A birth is considered preterm if it occurs before 37 weeks gestation.[34] Preterm birth is one of the leading causes of perinatal mortality in industrialized countries,[34] and affects approximately 8.1% of live births in Canada each year.[35] Infants born preterm are more likely to die during their first year of life, suffer from chronic illness, slow growth, and behavioural and learning difficulties than infants born full-term.[36] Preterm birth is more likely to occur in multiple (as opposed to singleton) births, when mothers have co-morbidities such as diabetes or hypertension, and to mothers that have had previous preterm deliveries.[35]

According to Miller, preterm birth accounts for the largest proportion of excess risk associated with short birth intervals.[37] A meta-analysis of 8 studies performed by Conde-Agudelo et al. supports this assertion, finding a significant increase in risk for preterm birth following a short interpregnancy interval. Pooled adjusted results show that risk for preterm birth is 40% higher in infants born after an interpregnancy interval of 6 months or less, compared with 18-23 months (OR: 1.40; 95% CI: 1.24, 1.58), controlling for maternal age and socioeconomic status.[3] Pooled unadjusted results found infants conceived after a short interpregnancy interval to be nearly 80% more likely to experience preterm birth (OR: 1.77; 95% CI: 1.54, 2.04).[3] This relationship has been demonstrated repeatedly in the literature.[29,38-46]

Low Birthweight

An infant is said to be low birthweight if they measure less than 2,500 grams (5 pounds 8 ounces) at birth.[35] This occurs either because they are born preterm, or because they are small for gestational age,[3] and affects about 6% of live births in Canada each year.[35] Low birthweight is often used as a marker of overall perinatal health because it has such strong ties with infant development, survival, and health. Infants born weighing under 2,500 grams are more likely to experience physical and cognitive disabilities, and chronic health problems across the lifespan.[35]

Etiologic studies have also found that short interpregnancy intervals have a causal relationship with low birthweight births.[38,42] In a meta-analysis of 6 studies controlling for maternal age and socioeconomic status, infants born after an interpregnancy interval of 6 months or less were 60% (OR: 1.61; 95% CI: 1.39, 1.86) more likely to be low birthweight according to unadjusted results, and over 200% (OR: 2.12; 95% CI: 1.98, 2.26) more likely according to adjusted results.[3]

Small for Gestational Age

There are a number of common characterizations of the term 'small for gestational age' (SGA), which is also analogous to intrauterine growth restriction/retardation (IUGR). Definitions include birth weight less than the 10th percentile for gestational age; birth weight less than 2 standard deviations below the mean value for gestational age; and birth weight less than 2,500 grams and gestational age greater than or equal to 37 weeks.[47] Yearly, about 8.3% of live births in Canada are SGA.[35] The most common maternal characteristics associated with SGA include maternal hypertension and primigravida (being pregnant for the first time). Several socio-demographic factors are also associated with SGA, including neighbourhood income and living in an urban setting.[35]

The relationship between SGA and short interpregnancy intervals is not consistent, though several studies have found a significant link.[43,44] Conde-Agudelo conducted a meta-analysis of 7 studies measuring small for gestational age, and found that infants born after an interpregnancy interval of 6 months or less were nearly 40% (OR: 1.39; 95% CI: 1.20, 1.61) more likely to be SGA than infants born after an interval of 18-23 months, according to unadjusted results. Adjust results showed they were closer to 30% (OR: 1.26; 95% CI: 1.18, 1.33) more likely to be SGA.

Perinatal Death

Perinatal mortality refers to stillbirths after 28 weeks and newborn deaths before 1 week of age.[48] The perinatal mortality rate has declined in recent years in Canada, from 6.8 in 1991 to 6.1 deaths per 1,000 total births in 2006."[48] The association between perinatal death and short interpregnancy intervals is not well supported in the literature,[3] though some studies have found an association.[43,49,50] A study of over 1 million births using 1991 U.S. Linked Birth-Death files from the American National Centre for Health Statistics found a statistically significant relationship between an interpregnancy interval of 6 months or less and perinatal death among white (OR: 1.20; $p<0.01$) and black (OR: 1.25; $p<0.01$) mothers.[49] Several other studies did not find a statistically significant association.[50]

2.1.4.2 Maternal Health

Preeclampsia

Preeclampsia is characterized by a rapid rise in blood pressure, protein in urine and swelling, and is a precursor of eclampsia, which causes tonic-clonic (full-brain) seizures. It is thought to be causally associated with nearly 15% of preterm births.[51] Preeclampsia affects 2.6%

of Canadian pregnancies, and approximately 1 in 200 of cases go on to become full eclampsia.[52] The causes of preeclampsia are not well established, though mothers tend to be over 40 or under 20, experiencing their first pregnancy, of black or Aboriginal ancestry, overweight, or have pre-existing high blood pressure, diabetes or kidney disease.[52]

Analyses of the relationship between short interpregnancy intervals and preeclampsia most often show a relationship between the two. Trogstad et al., in a study of 547,238 Norweigan women, found that birth-to-conception intervals of 12 months or less are associated with a 50% (OR: 1.5l; 95% CI: 1.2-1.9) increase in the occurrence of preeclampsia compared to those with intervals of 18 to 23 months, adjusting for age, previous preeclampsia, change of partner and year of second delivery.[53] Similar results have been found in North and South America.[54-56]

Maternal Death

The occurrence of maternal death, which is defined as non-accidental death during pregnancy or up to 42 days after the termination of pregnancy,[57] has declined substantially in the past century. In 1920, approximately 500 per 100,000 live births in Canada ended in maternal death, compared to less than 5 per 100,000 in the 1990s.[58]

The relationship between short interpregnancy intervals and maternal death has not been studied in depth. But, Conde-Agudelo and Belizan found that, after adjusting for confounding factors, women who conceive within 5 months of index birth had significantly increased rates of maternal death (OR: 2.54; 95% CI: 1.22, 5.38) compared to those with birth to conception intervals of 18 to 23 months.[55]

In addition to the outcomes discussion above, there is limited research available on the relationship between short interpregnancy intervals and other maternal outcomes such as premature rupture of membranes, gestational diabetes, third trimester bleeding, postpartum

hemorrhage and infection,[4] third trimester bleeding, premature rupture of membranes, puerperal endometritis, and anemia,[55] as well as childhood outcomes in offspring such as cerebral palsy,[59] schizophrenia,[60] and school readiness.[61] To date, these relationships are not well established.

2.1.5 Predictive Studies

Despite well-established risk to infants and mothers, few studies have attempted to develop predictive models to determine which women are at greatest risk of experiencing a short interpregnancy interval. Only two could be identified. The first was developed using 2,904 mothers in Denmark, and used logistic regression to determine determinants of becoming pregnant within nine months of previous birth using data from a national registry.[62] Short interpregnancy intervals, using a nine-month cut point, occurred in 4.8% of their sample and were more likely to occur as a result of an unplanned pregnancy (OR: 2.9; 95% CI: 2.2, 3.9), to follow irregular menstruation (OR: 1.7; 95% CI: 1.1, 2.5) and to high parity mothers (OR: 1.9; 95% CI: 1.1, 3.1). Poor housing, smoking and low socioeconomic status were also associated with birth intervals of nine months or less.[62]

The second was a study of 20,028 women receiving welfare in Washington State using the Washington State Needs Assessment Database.[63] Cox-proportional hazard modelling was used to identify individual- and community- level predictors of interpregnancy intervals up to seven years after birth. Factors such as age, education, race, marital status, and the interaction between age and gravida were statistically significant, but the model was shown to have little predictive power when validated using data-splitting.[63]

2.1.5.1 Research Gap

A common criticism of models developed to predict short interpregnancy intervals is that they may be closely bound to the source population. Neither Kaharuza et al. nor Gold et al. were able to fully evaluate the generalizability of their model in other populations.[62,63] Development of a specialized model may be especially important for use in clinics that serve a specialized population, such as the LIHC.

A key contribution of this project to the literature on short interpregnancy intervals will be the development of a clinical tool. The nomogram can be used to help clinicians predict which women are at greatest risk of conceiving again within 6 month of previous birth. This is a significant contribution because, though informative in a research setting, results from regression analyses are difficult to interpret and apply in a clinical setting.

3 CHAPTER THREE: OBJECTIVES

The purpose of this project is to enhance the capacity of the London Intercommunity Health Centre (LIHC) to provide preventative care to patients from underserved populations.

Project objectives are twofold:

1) To develop a model to predict which women using the LIHC's prenatal program are at greatest risk of experiencing a short interpregnancy interval using data routinely collected in Ontario prenatal clinics.

2) To create a user-friendly method for applying these findings in a clinical setting through the development of a predictive nomogram.

The results of this study may be generalized to other prenatal clinics that serve similar population groups.

4 CHAPTER FOUR: METHODS

It should be noted that every attempt was made to avoid disturbing the prenatal clinic over the course of study completion. Data already collected in clinics across Ontario was used to minimize burden, and to make tools as user friendly as possible. This allowed for quality data to be collected with little disruption to the clinic, ensured that the use of the model could be sustained, and maximized the utility of results.

4.1 Design

This study uses a retrospective case-control design. Those with short interpregnancy intervals (cases) are compared to those with moderate interpregnancy intervals (controls) on a variety of social and biological characteristics. The resulting model will be predictive, as variables in the model will be used to identify those at greatest risk of experiencing a short interpregnancy interval, and will not provide information on causality.

4.1.1 Study Population

Participants were patients of the prenatal program at the London Intercommunity Health Centre (LIHC) in London, Ontario. The LIHC provides services to this population via two locations in London's east side, which house many of the city's newest and poorest residents. The LIHC patient base is ethnically heterogeneous, representing 79 countries of origin and 36 different languages, but economically homogeneous, as 63% of clients with annual household income less than $19,999.[1]

Patients were referred for participation based on appointment records between January 2000 and December 2008. All data was retrieved from paper medical records, and participants were never contacted for additional information. As such, informed consent was not obtained. A

consent waiver was granted by the Health Sciences Research Ethics Board at The University of Western Ontario because of the absence of physical, emotional, or psychological danger to participants; the inability to identify characteristics of individual patients from aggregated data; and the lack of ongoing relationship of participants with the clinic due to the temporary nature of prenatal care (see appendix A).

4.1.1.1 Inclusion Criteria

Patients were eligible to participate if they attended at least one prenatal appointment at the LIHC between January 2000 and December 2008, if their current pregnancy was not their first, and if one or more of their previous pregnancies resulted in live or still birth, as opposed to spontaneous or therapeutic abortion, which occurs before 24 weeks gestation.

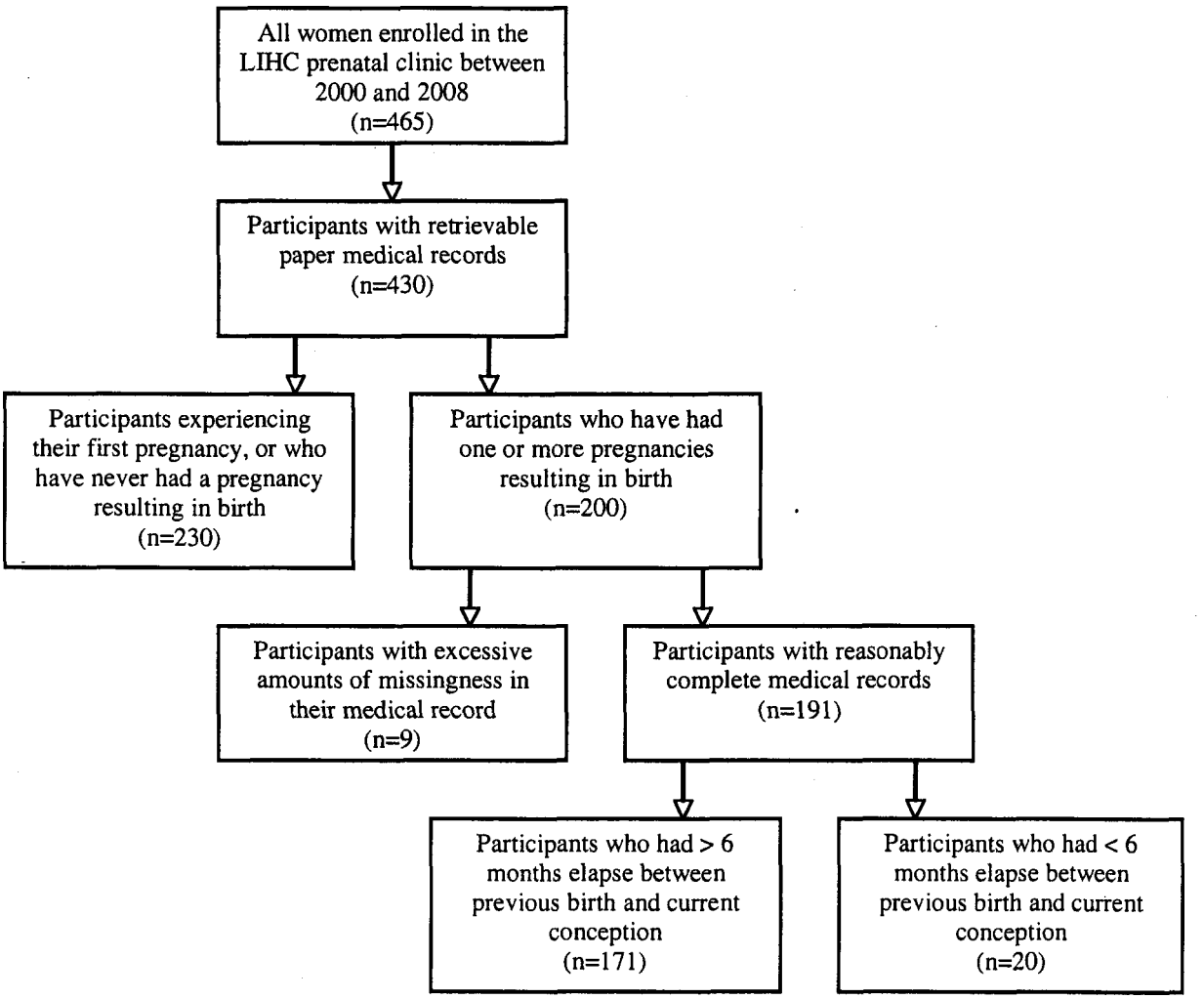
4.1.1.2 Exclusion Criteria

Patients were excluded if their medical records were excessively incomplete, particularly if there was inadequate information available on dates or outcomes of previous pregnancies.

4.1.1.3 Sample Size

In total, 465 patients were referred for participation based on clinic appointment schedules. Ninety-two percent (n=430) of paper-based medical records were located, and 46.5% (n=200) of patients whose charts were located met the inclusion criteria. Due to excessive amounts of missing information, 9 charts were dropped from the analysis. The final sample consisted of 191 participants. Ten-and-a-half percent (n=20) of participants were classified as cases, while 89.5% (171) were classified as controls. See figure 4.1 for a graphical representation.

Figure 4.1: Sample schematic



4.1.2 Data Source

The data used in this analysis were retrieved from LIHC medical records, which are currently in paper format. All variables were abstracted by the student researcher and entered into a Microsoft Access database.

Variables were collected from two forms. The 'Ontario Medical Association/Ontario Ministry of Health and Long-Term Care Antenatal Record 1' (see appendix B), a government-

mandated form that is filled out in prenatal clinics across the province of Ontario, served as the primary source of data. This information was supplemented by variables collected from the 'London Intercommunity Health Centre Client Intake Form' (see appendix C).

4.1.3 Collected Variables

All reasonably complete variables suspected to have predictive relevance were collected. They can be loosely categorized into socio-demographic, behaviour and bio-medical predictors. For a complete list of variables in each category, see tables 4.1, 4.2 and 4.3.

Table 4.1: Complete list of socio-demographic variables collected

Variable	Code	Source	Levels
Immigration status	ImmGrp	LIHC intake	1=Canadian citizen 2=Landed immigrant, permanent resident, visitor 3= Refugee, illegal
English speaking	EngSpk	LIHC intake	1=Yes 2=No
Country of origin (by broad category)	OrCode	Both	1=Canada, US, Caribbean* 2=Europe 3=Latin America 4=Africa 5=South West Asia, West Asia, South Asia 6=South East Asia
Aboriginal Canadian	AborCan	Antenatal	1=Yes 2=No
Education level	EduGrp	LIHC intake	1=College, University, or Part University 2=Highschool Complete, Part Highschool 3=Elementary Complete, Part Elementary, No Formal Education
Household income	Income	LIHC intake	1=0-14,999 2=15,000-19,999 3=20,000-24,999 4=25,000-29,999 5=30,000+
Occupation specified	OccYN	Antenatal	1=Specified Employment 2=No Specified Employment
Marital status	Martial	Antenatal	1=Single 2=Common Law 3=Separated 4=Married
Poor social support (self-identified)	PoorSS	Antenatal	1=Yes 2=No
Homelessness (self-identified, at time of last pregnancy)	Home	Both	1=Yes 2=No
Any information provided on father, including age, occupation and education	FathInfo	Antenatal	1=Any Father Information Provided 2=No Father Information Provided

*Caribbean patients were categorized with Canada and the United States for geographic reasons (as a member of North America) in the absence of a close cultural match.

Table 4.2: Complete list of behavioural variables collected

Variable	Code	Source	Levels
Smoking status (self-identified, at time of current pregnancy)	Smoke	Antenatal	1=Yes 2=No
Alcohol or drug use (self-identified, at time of current pregnancy)	AlcDrug	Antenatal	1=Yes 2=No
Indicated substance abuse problem (self-identified, at time of current pregnancy)	SubAb2	Antenatal	1=Yes, patient indicated substance abuse problem 2=Patient indicated no substance abuse problem, or did not answer
Indicated family violence (self-identified, at time of current pregnancy)	FamVi4	Antenatal	1=Yes, patient indicated family violence 2=Patient indicated no family violence, or did not answer
Involvement of the Children's Aid Society in care of children (self-identified, at time of current pregnancy)	CAS	Both	1=Yes 2=No

Table 4.3: Complete list of bio-medical variables collected

Current age	Age	Antenatal	N/A (continuous)
Index age (age as of index pregnancy)	AgeAdj	Antenatal	N/A (continuous)
Total number of pregnancies	Gravida	Antenatal	N/A (continuous)
Number of previous pregnancies before current	GravAdj	Antenatal	N/A (continuous)
Number of pregnancies carried to term (≥37 weeks)	Term	Antenatal	N/A (continuous)
Number of pregnancies delivered prematurely (<37 weeks)	Premat	Antenatal	N/A (continuous)
Number of lost pregnancies (spontaneous or through terminating abortion)	Abortus	Antenatal	N/A (continuous)
Experience of 1 or more stillbirths (occurring after 28 weeks gestation)	Still2	Antenatal	1= ≥ 1 stillbirths 2= No stillbirths
Number of living children	Living	Antenatal	N/A (continuous)
Experience of a previous short interpregnancy interval (≤ 6 months)	PrevIPI	Antenatal	1=Yes 2=No
Psychiatric diagnosis (by broad category)	PsyCat	Antenatal	1=None 2=Depression 3=Other diagnosis

4.1.4 Variable Measurement

4.1.4.1 Outcome Variable

An interpregnancy interval is the time that passes between still or live birth and next conception, based on date of birth and last menstrual period. Stillbirth is distinguished from

spontaneous abortion or miscarriage at 24 weeks gestation. A short interpregnancy interval is an interpregnancy interval of six months or less. This study examines the occurrence of a short interpregnancy interval in participant's most recent pregnancy.

4.1.4.2 Predictor Variables

Continuous

Categorization of continuous variables was avoided to prevent any loss of information.[64] All continuous variables were modelled using quadratic terms to ensure flexibility when a linear relationship is inadequate. Quadratics were only retained in the final model when statistically significant.

Categorical

Categorical variables were collapsed into fewer categories when appropriate to conserve degrees of freedom, and modelled using dummy variables.

4.2 Statistical Analysis

The analysis techniques used in this study were chosen specifically to deal with the challenges that arise when working with a small sample. The goal was to make the results as generalizable as possible by avoiding data dependency; that is, trying to ensure the results do not depend on this particular data set.

4.2.1 Model Type

The outcome of interest is binary, comparing those who experienced a short interpregnancy interval in their most recent pregnancy with those who did not. Therefore, logistic regression was employed. This model has several advantages over other techniques,

including that few distributional assumptions are made, and results lend themselves to easy interpretation through the provision of odds ratios.[65]

4.2.1.1 Model Assumptions

Linearity

In logistic regression, it is assumed that each predictor is linearly related to the log odds of outcome.[64] This assumption is of no concern for categorical variables, and was assessed in continuous variables by introducing quadratic and higher-level terms into the model.

Collinearity

A key concern when using stepwise variable selection is ensuring that variables are not highly correlated, or collinear. If collinear variables are left in the model, variable selection is made arbitrary because variables representing the same phenomena are competing for spots in the model.[66] As a result, regression coefficients become difficult to interpret because there is inadequate information on the effect of one variable when it is assumed that all other variables in the model are controlled for.[66] In this analysis, the collinear relationship between variables was assessed using the VARCLUS procedure in the R Design library.

4.2.2 Missing Data

Careful treatment of missing data is essential to the validity of any regression model. Because the results of this study are intended for application in clinical settings, extra care had to be taken to select variables that would be available without placing an additional burden on the clinic, or requiring extensive imputation. Techniques for dealing with missing data were selected based on the magnitude of missingness.

4.2.2.1 Single Imputation

A number of candidate variables (n=9) had between 0.5% and 5.7% missingness. Based on a series of simulation studies, Harrell found that when missingness is 5% or less, an analyst's choice of imputation technique will not have an effect on the fit of the model.[66] When this condition is met, he advocates imputing the median value in the case of categorical variables, and the mean value in the case of continuous variables, a strategy known as 'single imputation.' The small proportion of missingness circumvents concerns with single imputation, namely the underestimation of variance and standard error, which biases regression coefficients.[67]

Assuming that 5% is a relatively arbitrary cut point, this rule has been extended to variables with up to 5.7% missingness. For a complete list of variables affected by single imputation, see table 4.4.

Table 4.4: Summary of missingness in variables affected by single imputation

Psychiatric diagnosis by category	PsyCat	1.6
Marital status	Martial	0.5
Previous short interpregnancy interval	PrevIPI	6.2
Homelessness	Home	1.6
Alcohol or drug use	AlcDrug	3.7
Relationship problems	RelatProb	5.7
Poor social support	PoorSS	4.1

4.2.2.2 Variable Redefinition

Several collected variables (n=5) had large amounts of missingness but were still desirable as part of the model. In some circumstances, missingness itself was seen as valuable information, so variables were redefined to accommodate missingness.

All variables relating to paternal relationships - including the father's age, income, and occupation - were collected with substantial missingness (between 36.1% and 89.0%). This

missingness does not appear to be random, and appears to be 'non-ignorable' (meaning that there is a connection between the occurrence of missingness and the value of the variable).[67] In this particular population, a lack of paternal information, or an unwillingness to share this information, may be informative in itself. Therefore, all three paternal variables were recoded together as a binary variable: any fatherly information provided (yes/no).

The same strategy was used for substance abuse problems (a substance abuse problem was indicated [yes/no]), and family violence (family violence was indicated [yes/no]). In these cases, 'no' does not necessarily mean that there is an absence of substance abuse problems or family violence, but rather that it was not indicated. See table 4.5 for details.

Table 4.5 Summary of missingness in variables that were redefined

Father's occupation	FathOcc	66.5
Father's education	FathEdu	89.0
Father's age	FathAge	36.1
Indicated substance abuse problem	SubAb	6.2
Indicated family violence	FamViol	12.0

4.2.2.3 Exclusion

One variable was excluded from the analysis for excessive missingness with no possibility of redefining or imputing missing values: contraceptive use and type. With 46.6% missingness, this variable was not routinely collected and it is likely that it will not be routinely collected in future patients, making it an unstable predictor.

Two variables, income and education, had a moderate amount of missingness (15.7% and 14.1% respectively), but posed problems in terms of imputation (see table 4.6). Though both variables intuitively seem as though they may be good candidate predictors, they were excluded from the final model for different reasons.

Income was excluded from the model due to a lack of variability. 92% of participants had a personal income of $14,999 or less, which is the lowest income group collected. This homogeneity meant that this variable was not a good candidate for a more complex imputation technique, and that it was unlikely to be a good predictor.

Education was excluded after conducting a complete case analysis, an analysis based only on cases where the variable was available,[68] and finding no association between the variable and the outcome of interest. If an association had been found, a more complex imputation methods such as multiple imputation would have been performed.

Table 4.6: Summary of variables deleted from the model due to problematic missingness

Income	Income	15.7
Education level	Edu	14.1

4.2.3 Bivariate Analysis

4.2.3.1 Continuous Predictors

The independent association between each continuous predictor and the outcome variable was assessed using t-tests. Predictor variables with a p-value of 0.5 or less were entered into the multivariable model. $P<0.5$ was chosen as a cut-point in order to narrow down the number of variables initially entered into the model by eliminating variables with little to no crude association with the outcome.

4.2.3.2 Categorical Predictors

The independent association between each categorical predictor and the outcome variable were assessed using Pearson's chi-square tests. As with continuous variables, predictors with a p-value of 0.5 or less were entered into the multivariable model.

4.2.4 Variable Selection

It is important to pare down the number of variables used in the final model further to avoid marrying the model too closely with the idiosyncrasies of this particular dataset, a problem related to the concept of 'overfitting.'[64] The goal was to identify trends that best describe the phenomena in general, as opposed to what is happening in this sample population.[64]

In order to avoid overfitting, Harrell suggests aiming for roughly $m/10$ predictor degrees of freedom, where m is the number of events or cases, and degrees of freedom are based on the number of continuous variables and the number of levels of categorical variables.[64]

There are a variety of variable selection techniques available that are aimed at determining the best subset of variables to use in the final model depending on the specific aims of the analysis. This project aimed to predict which women are at greatest risk of experiencing a short interpregnancy interval based on variables already collected by the LIHC prenatal clinic and other Ontario prenatal clinics.

Since the literature on significant predictors of short interpregnancy intervals is sparse, backward elimination stepwise variable selection was employed. Despite the recent decline of 'deterministic' modes of variable selection, this method was preferential because all variables are given equal footing and are then eliminated based on importance, as specified by a pre-determined decision rule. This occurs without any prior knowledge of significant associations.[69]

In this case, variables were eliminated from the model based on a p-value cut-point of 0.25 in one model, and 0.1 in the next. These levels were chosen in order to sufficiently limit the number of predictors in the model while avoiding eliminating important variables prematurely, which can occur when using the traditional p-value of 0.05.[69]

4.2.5 Performance Evaluation

In order to assess the quality of the model, several techniques were used that assess predictive accuracy, namely discrimination and calibration.

4.2.5.1 Discrimination

Discrimination refers to the model's ability to accurately distinguish between cases and controls. In this analysis, discrimination was assessed using a measure of concordance, otherwise known as the c-index.[65] The c-index is equivalent to the area under a receiver operator characteristic (ROC) curve, which plots sensitivity (true positives) against 1-specificity (true negatives). A c-index of 0.5 indicates a complete absence of predictive discrimination, while a c-index of 1.0 indicates perfect sensitivity and specificity. A c-index of 0.8 is conventionally considered good discrimination.[66]

4.2.5.2 Calibration

In order to assesses reliability, that is, to determine how well the model is able to estimate the outcome in an unbiased manor, calibration was used.[66] After bootstrapping the sample 1,000 times, reliability was measured by determining whether there is agreement between predicted and observed probabilities. This was done by comparing the observed and biased corrected slope to the ideal slope.[65] Ideal calibration is indicated by an intercept of 0 and a slope of 1. If the intercept is less than 0, predicted probabilities are too low on average, and if it is above 0 predictions are too high. A slope of less than 1 indicates that the regression coefficients were biased toward the extreme (either high or low) on average, and a slope greater than 1 indicates they were biased toward to zero. These estimates were obtained using the VALIDATE function

in the R Design library, and will be displayed graphically using the CALLIBRATE function in the R Design library.

As a reference, bootstrapping is a technique that offers information about the population the sample originated from by creating a set number of new samples from the original sample by drawing with replacement.[65] In this example, 1,000 unique samples of 191 participants were created by drawing with replacement from the original 191 participants. Bootstrapping is preferred over techniques such as data-splitting, which develops the model on half of the sample and tests it on the other half, because of its use of the entire sample for both the development and assessment of the model.[64]

4.2.6 Clinical Application

4.2.6.1 Nomogram

As specified in research objective 2, an important element of this project was to provide the LIHC and other health centres with a practical tool to apply the results of this analysis in their prenatal clinic. Given that the LIHC prenatal clinic has not yet fully transitioned to an electronic charting system, a paper-based tool in the form of a predictive nomogram is appropriate. The nomogram will allow clinicians to calculate an individual patient's risk of experiencing a short interpregnancy interval with ease using the predictors deemed most important in the logistic regression model.

5 CHAPTER FIVE: RESULTS

5.1 Descriptive Statistics

5.1.1 Descriptive Statistics of Full Sample

In total, 191 patients were included in the final analysis. The average age of participants at most recent birth was 25.23 (SD +/-5.84), and ranged from 13 to 42. The average age at current pregnancy was 28.51 (SD +/- 6.20), and ranged between 17 and 44. In accordance with the inclusion criteria, all patients included in the study had at least one pregnancy resulting in live birth, but participants had an average gravida of 3.01 (SD +/- 2.27), ranging from 1 to 12 before current pregnancy. Participants had between 0 and 7 living children, with an average of 2.12 (SD +/- 1.45).

As indicated in table 5.1, the greatest proportion of participants (41.05%) were married at the time of most recent pregnancy. 32.63% were single, 22.11% cohabitating, and 4.21% were separated. There was very little variability in the yearly personal income of participants. Only 7.45% (n=12) of participants indicated having a yearly personal income $15,000 or greater in the year before current pregnancy. The majority (55.5%, n=132) of participants had at least some high school education, while 2.44% (n=4) had no formal education, and 19.5% (n=32) had some post-secondary education.

The vast majority of participants (78.95%, n=150) speak at least some English, and 52.91% (n=100) speak English only. Most participants (64.64%, n=117) were Canadian citizens, 47 (25.96%) were permanent residents; 1 participant (0.55%) held a visitor's visa; 15 participants (8.29%) held refugee status; and 1 participant (0.55%) had no legal status in Canada.

Only 46.03% (n=87) of participants were born in Canada. Patients included in this sample came from 42 countries in five continents and spoke 19 languages. Of those born in Canada, 15 (17.24%) participants identified as Aboriginal Canadian. Thus, Aboriginal Canadians constitute 7.89% of the total sample. Overall, nearly half (49.73%, n=93) of participants originated somewhere in North America. 8.56% (n=16) came from South America, 19.79% from Asia, 14.97% from Africa, and 6.95% from Europe. To see a complete breakdown of continent and country of origin, see appendix D.

Table 5.1: Descriptive statistics - full sample

Marital Status (n=190)		
Married	78	41.05
Common law	42	22.11
Separated	8	4.21
Single	62	32.63
Yearly Income (n=161)		
$0 – $14,999	149	92.55
$15,000 – $19,999	9	5.59
$20,000 – $24,999	1	0.62
$25,000 – $29,999	0	0
$30,000 – $34,999	1	0.62
$35,000 – $39,999	1	0.62
Highest Level of Education Attained (n=164)		
No Formal Education	4	2.44
Some Elementary	3	1.82
Elementary Complete	25	15.24
Part High School	41	25.00
High School Complete	59	35.98
Some College	17	10.37
Some University	15	9.15
Immigration Status (n=181)		
Canadian Citizen	117	64.64
Permanent Resident	47	25.96
Visitor Visa	1	0.55
Refugee	15	8.29
Illegal	1	0.55

5.1.2 Descriptive Statistics of Cases

Women who experienced a short interpregnancy interval between their most recent birth and subsequent pregnancy were, on average 26.30 years of age (+/-6.97) at last birth, and 26.45 (SD +/- 6.81) at current pregnancy, compared to 25.11 (SD +/-5.70) in controls. Cases had an average of 3.20 (SD+/- 2.06) previous pregnancies, ranging between 1 and 9, compared to 2.98 (SD +/- 2.29, range 1 to 12) in controls. They had an average of 2.3 (SD +/- 1.62) living children, ranging from 0 to 6.

Thirty-five percent (n=7) of patients identified as cases were in a common law relationship at current pregnancy. Twenty five percent (n=5) were married, 10% (n=2) were separated, and 30% (n=6) were single. Similar to the total sample, there was very little variability in the yearly personal income of cases. Only 1 participant earned more than $14,999, reporting an income of $15,000-19,999. Fifty percent (n=9) of cases had attained at least some high school education. At the extremes, 1 case had no formal education, and 2 had some university or college education.

Seventy percent (n=14) of participants identified as cases speak English, while 30% (n=6) did not. Approximately 63% (n=12) were born with or have attained Canadian citizenship, 21.05 (n=4) had permanent resident status, and 5.26% (n=3) were either refugee claimants or held no legal status. Cases born outside of Canada came from 9 different countries and spoke 5 different languages. Twenty percent (n=2) of cases born in Canada identified as being Aboriginal Canadian. For a complete profile of continent and country of origin among cases see appendix E.

Table 5.2: Descriptive results - cases

Marital Status (n=20)		
Married	5	25
Common law	7	35
Separated	2	10
Single	6	30
Yearly Income (n=18)		
$0 – $14,999	17	94
$15,000 – $19,999	1	6
$20,000 – $24,999	0	0
$25,000 – $29,999	0	0
$30,000 – $34,999	0	0
$35,000 – $39,999	0	0
Highest Level of Education Attained (n=19)		
No Formal Education	1	5.6
Some Elementary	0	0
Elementary Complete	4	22.2
Part High School	4	22.2
High School Complete	7	38.9
Some College	1	5.6
Some University	1	5.6
Immigration Status (n=19)		
Canadian Citizen	12	63.2
Permanent Resident	4	21.1
Visitor Visa	0	0
Refugee	2	10.6
Illegal	1	5.3

5.2 Model-Based Results

5.2.1 Checking Model Assumptions

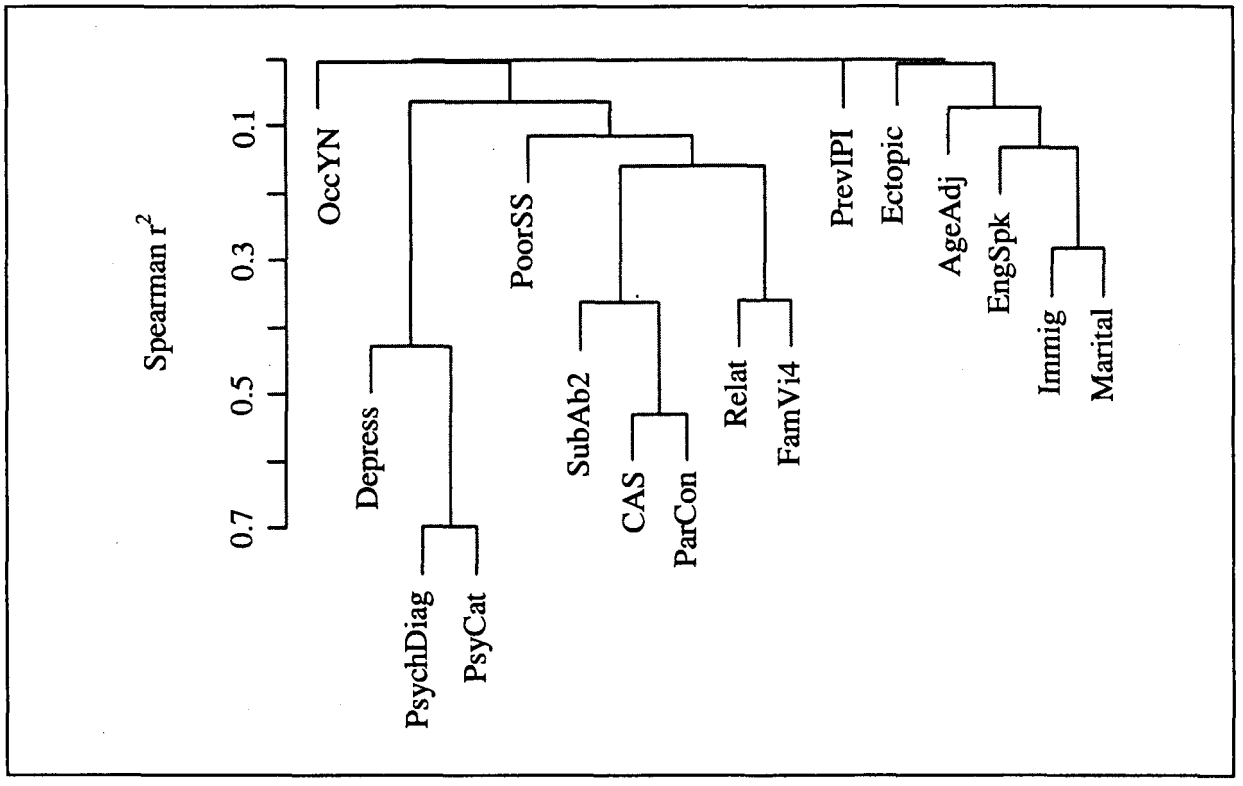
5.2.1.1 Linearity

The only continuous variable entered into the final model was age at last birth. The linearity assumption was assessed by adding age^2, a quadratic term, into the model. This was not significant, and did not improve the fit of the model. Therefore, linearity was assumed.

5.2.1.2 Collinearity

Created using the VARCLUS procedure in the Design library of R, figure 5.1 demonstrates the relationship between all variables and the level of correlation, measured using squared Spearman rank correlation coefficients, which can be seen along the Y-axis.

Figure 5.1: Collinear relationship between variables



Based on figure 5.1, depression status (Depress) and category of psychiatric diagnosis (PsyCat) were removed from the model because they were highly correlated (ρ^2=~0.7) with occurrence of psychiatric diagnosis (PsychDiag). Occurrence of psychiatric diagnosis was chosen over they other two variables because of its significant association with the outcome variable. Identified parenting concerns (ParCon) was also deleted due to excessive correlation with the presence of Children's Aid Society in the care of living children (CAS).

Table 5.3: Bi-variate associations in continuous predictors using t-tests

Current age	189	-2.30	0.12*
Index age	189	1.19	0.39*
Gravida	189	0.21	0.69
Number of pregnancies carried to term	189	0.14	0.68
Number premature	189	0.02	0.84
Number of abortuses	189	0.01	0.97
Number terminated	20.4**	0.14	0.53
Number of spontaneous terminations	30.3**	0.08	0.65
Number of stillborns	30.1**	-0.02	0.72
Number living	189	0.21	0.55

*Significant at P<0.5 level

**Degrees of freedom have decimal places because they were conducted using t-tests for unequal variances

5.2.2.2 Categorical Predictors

Categorical variables were examined separately using chi-square tests. Immigration status (Immig); ability to speak English (EngSpk); involvement of the Children's Aid Society (CAS); employment indicated (OccYN); marital statuts (marital); previous short interpregnancy interval (PrevIPI); having poor social support (PoorSS); having a diagnosis of depression (Depress); identifying as having a substance abuse problem (SubAb/SubAb2); identifying as experiencing family violence (FamVi/Fam4); having parenting concerns (ParCon); having a psychiatric diagnosis (PsychDiag); and psychiatric diagnosis by major category (PsyCat) were statistically significant at p<0.5. Results are listed in table 5.4.

Table 5.4: Bi-variate associations in categorical predictors using chi-square tests

Immigration status	6	9.05	0.17*
English speaking	1	1.11	0.29*
Country of origin	5	2.07	0.84
Aboriginal Canadian	1	0.14	0.71
Education	7	2.72	0.91
Income	4	0.36	0.99
Children's Aid Society	1	4.38	0.04*
Occupation specified	1	2.16	0.14*
Marital status	3	5.01	0.17*
Fatherly information	1	0.00	0.97
Stillborn birth	1	0.00	0.96
Previous short IPI	1	4.55	0.03*
Smoking status	1	0.00	0.98
Alcohol or drug use	1	0.31	0.58
Poor social support	1	1.61	0.20*
Depression	1	1.04	0.30*
Substance abuse problem	1	3.42	0.06*
Indicated substance abuse problem	1	4.15	0.04*
Family violence	1	2.50	0.11*
Indicated family violence	1	2.02	0.16*
Parenting concerns	1	1.84	0.17*
Psychiatric diagnosis	1	2.45	0.12*
Psychiatric diagnosis by type	2	1.43	0.49*
Homelessness	1	0.06	0.81

*Significant at P<0.5 level

5.2.3 Variable Selection

Backwards step-wise elimination was first performed with a cut-point for inclusion of $p<0.25$ to allow the maximum number of significant variables to work together in forming the final set of variables entered into the model. Two variables were removed as a result. The model produced by this variable selection cut-point is referred to as 'Model 1.'

In order to limit the number of variables entered into the final model and avoid overfitting, backwards elimination was re-run with a cut-point for inclusion of $p<0.1$. Using this criterion, four variables were eliminated. The model produced using this cut-point will be referred to as 'Model 2.'

5.2.4 Main Effects Model 1

Model 1 was created using all variables that met the $p<0.5$ cut-point in the bivariate analysis, and was trimmed down further using backwards elimination with a cut-point of $p<0.25$. According to this analysis, the odds of experiencing a short interpregnancy interval are 13.88 times greater for refugee claimants or illegal immigrants as Canadian citizens (95% CI: 1.59, 121.15), holding all other variables in the model constant, and women who are common law as opposed to married are 7.94 more likely to experience a short interpregnancy interval (95% CI: 1.17, 54.09). Women who had an identified occupation were less likely to experience a short interpregnancy than those with no specified occupation, holding all other variables in the model constant (OR: 0.23; 95% CI: 0.07, 0.81). See table 5.5 for details.

Table 5.5: Model 1 results: logistic regression

Immigration status		
Canadian citizen	1.00	--
Permanent resident	3.25	0.57, 18.38
Refugee/illegal	13.88	1.59, 121.15
Children's Aid Society	3.64	0.87, 15.16
Index Age	1.11	1.00, 1.23
Occupation specified	0.23	0.07, 0.81
Marital status		
Single	2.60	0.39, 17.46
Common law	7.94	1.17, 54.09
Separated	6.35	0.60, 67.47
Married	1.00	--
Previous short IPI	3.70	0.84, 16.39
Poor social support	2.18	0.63, 7.60
Psychiatric diagnosis	0.43	0.118, 1.55

5.2.5 Main Effects Model 2

Similarly, model 2 was created using all variables that met the $p<0.5$ cut-point in the bivariate analysis. But, to limit the number of variables allow into the model, backwards

elimination was employed with a more stringent cut-point of $p<0.1$. According to this analysis, the odds of experiencing a short interpregnancy interval are 10.56 times greater for refugee claimants or illegal immigrants as Canadian citizens (95% CI: 1.36, 81.70), holding all other variables in the model constant, and women who are common law as opposed to married are 7.16 times more likely to experience a short interpregnancy interval (95% CI: 1.43, 44.81). Similar to model 1, women who had an identified occupation were less likely to experience a short interpregnancy than those with no specified occupation, holding all other variables in the model constant (OR: 0.30; 95% CI: 0.10, 0.94).

In addition to the significant variables found in model 1, involvement of the Children's Aid Society was significant in model 2. Women with Children's Aid Society involvement were 4.93 times more likely to experience a short interpregnancy interval, compared to those without, holding all other variables in the model constant (OR: 4.93; 95% CI: 1.28, 18.72). See table 5.6 for details.

Table 5.6: Model 2 results: logistic regression

Immigration status		
Canadian citizen	1.00	--
Permanent resident	2.12	0.44, 10.15
Refugee/illegal	10.56	1.36, 81.70
Children's Aid Society	4.93	1.28, 18.72
Index Age	1.10	0.99, 1.21
Occupation specified	0.30	0.10, 0.94
Marital status		
Single	3.33	0.52, 21.40
Common law	7.16	1.43, 44.81
Separated	6.30	0.63, 63.18
Married	1.00	--
Previous short IPI	3.50	0.82, 14.89

5.3 Performance Evaluation

5.3.1 Discrimination

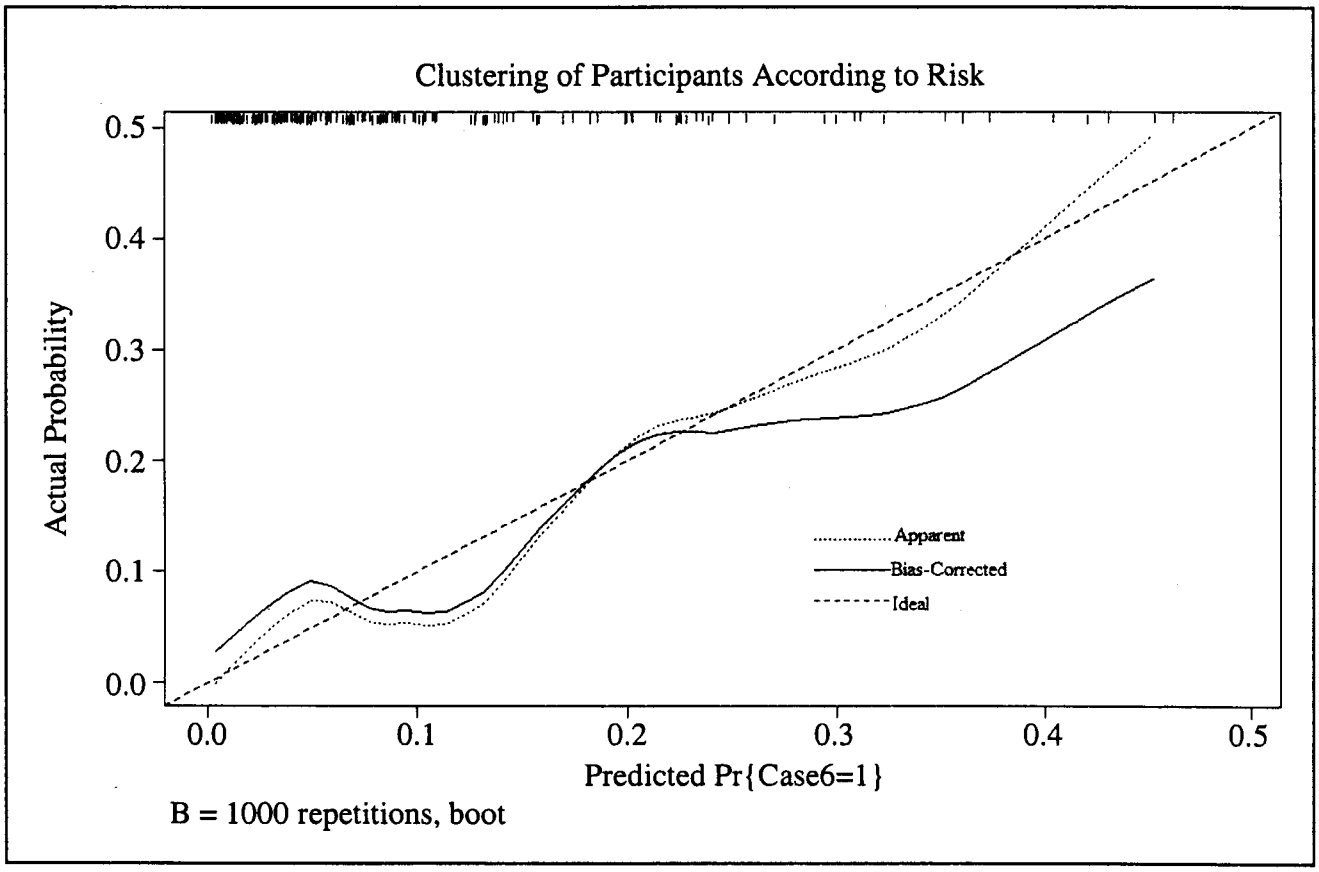
Predictive discrimination was assessed using the c-index. In model 1, the c-index was 0.797, and 0.781 in model 2. This indicates fair predictive ability, as good predictive ability is generally considered 0.8 or higher.

5.3.2 Calibration

Model 1

Bootstrapped results estimated the calibration intercept to be -0.82 in model 1, which indicates that predictions were high on average; as discussed above, the ideal calibration intercept is 0. The calibration slope is 0.52, when the ideal is 1, indicating that regression coefficients may be overestimated and results were pushed toward the extremes. The predictive accuracy of the model using 1,000 bootstrapped samples is displayed in figure 5.3. The line representing the ideal probability is the true probability; the line representing the apparent probability are the results of prediction on the original dataset; and the line representing the bias-corrected probability is applied on the new, bootstrapped datasets. The predicted probabilities rise above and fall below the ideal probability occurs because it is a smooth non-parametric curve.

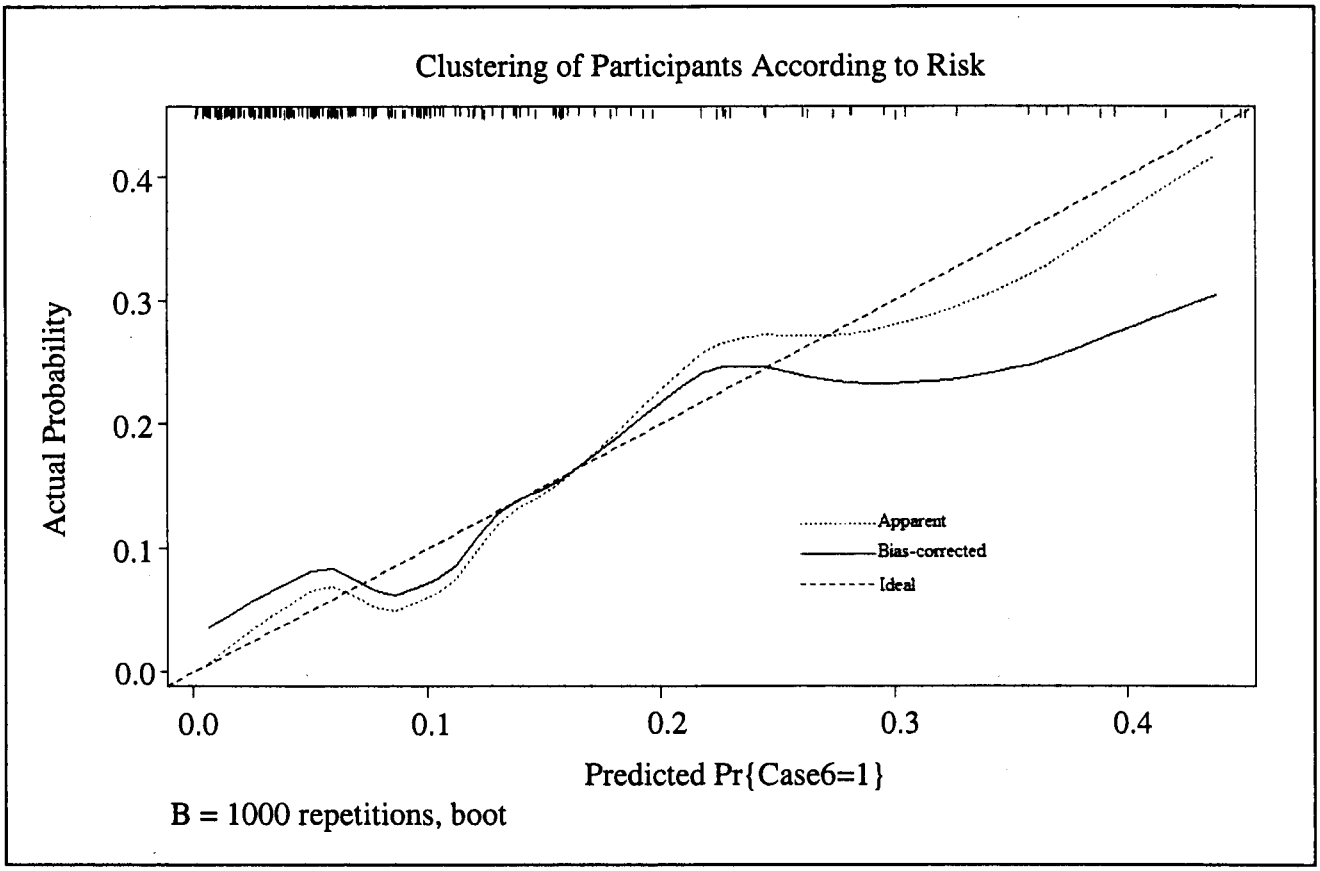
Figure 5.3: Predictive Accuracy of Model 1



Model 2

In model 2, bootstrapped results estimated the calibration intercept to be -0.78. The calibration slope is 0.57. As in model 1, this indicates that risk estimates are overestimated on average, and regression coefficients are overestimated, causing polarized risk estimates. The predictive accuracy of model 2 is presented in figure 5.4.

Figure 5.4: Predictive accuracy of model 2



5.4 Clinical Application

5.4.1 Nomogram

The predictive nomogram allows clinicians to determine the individual risk of becoming pregnant within 6 months of previous birth based on a variety of variables collected in routine practice. The nomogram is used by determining the point value of each variable by following the patient's response to the attributed value at the top of the nomogram. Total points are then tallied and the corresponding probability is given at the bottom of the nomogram. It is up to individual clinicians to determine the level of risk that warrants preventative action. The nomogram based on Model 1 is presented in figure 5.5, and the nomogram based on Model 2 is presented in figure 5.6.

Figure 5.5: Model 1 nomogram

To use: by determine the point value of each variable by following the patient's response to the attributed value at the top of the nomogram. Total points are then tallied and the corresponding probability is given at the bottom of the nomogram.

Figure 5.6: Model 2 nomogram
To use: determine the point value of each variable by following the patient's response to the attributed value at the top of the nomogram. Total points are then tallied and the corresponding probability is given at the bottom of the nomogram.

6 CHAPTER SIX: DISCUSSION

6.1 Discussion of findings

6.1.1 Bivariate and Multivariate Analyses

The goal of these analyses was to determine a subset of variables that identify women at risk of becoming pregnant within six months of giving birth using data already collected at the LIHC prenatal clinic. The individual variables and sets of variables that were shown to be the best predictors of short interpregnancy intervals must be interpreted cautiously, as we do not have sufficient information to make causal inferences.

Since there have been few studies looking at potential predictors of short interpregnancy intervals, it is difficult to determine why these predictors are statistically significant. It is possible that women that have previously experienced a short interpregnancy interval are at greater risk of experiencing another because they are choosing to have children closely spaced. This may be related to increased age, a variable that is approaching statistical significance, as it has been found in previous studies that women who delay childbearing tend to have significantly shorter birth-to-conception intervals.[70]

While the occurrence a previous short interpregnancy interval as a strong predictor is likely due to choice, it is possible that common-law status is a strong predictor of short interpregnancy intervals because of high rates of unintended pregnancies. This could be the case because many women in this group have never been married, which is a marker for risk for unintended pregnancy as discussed above.[23] This risk may be attenuated by the occurrence of regular sexual activity without concern for protection against sexually transmitted infections, which may compromise the use of contraceptive measures.

There are several possible explanations for why refugee status is a strong predictor of the occurrence of a short interpregnancy interval. The first is that attitudes toward birth control and family planning in the patient's country of origin or according to their religious beliefs may be prohibitive.[20] The second is that holding refugee status is an indicator that the patient has experienced a period of time without health care coverage, or with insufficient coverage, which would limit their ability to access contraceptive measures if they chose to.[71,72] Even health services directly aimed at refugees often omit family planning services because of the belief that refugee status is short-term, which is often not the case.[73]

It difficult to speculate why the involvement of the Children's Aid Society is a strong predictor of short interpregnancy intervals. Anecdotally, LIHC clinicians noted that some women who have had children removed from the home by CAS have chosen to have additional children quickly to have a fresh start at parenthood. But, given the highly collinear relationship between CAS involvement and other variables such as poor social support, parenting concerns and identified substance problems, it is also possible that the involvement of CAS actually identifies a particularly disadvantaged group of women that may have compromised reproductive autonomy[74] and higher rates of unintended pregnancies.[23]

It is difficult to understand and interpret many of the other variables in the model that were not statistically significant because the confidence intervals are wide, and the direction and magnitude of the associations are therefore unreliable. Further, it is not surprising that significant predictors found in this study were not analogous to previous predictive studies, as this analysis was conducted on a highly specialized population.

6.1.2 Model Performance

Overall, model 2 is preferable over model 1 due to the equivalence in performance, and benefits that arise from needing a fewer number of variables. Utilizing fewer variables means that there is less of a chance of missingness, and the nomogram is easier to apply because there are fewer scores to add.

Both model 1 and 2 demonstrated a level of discrimination that approached the standard cut-point for good discrimination, but both had predictive ability that was limited when applied to the bootstrapped sample. This is likely indicative of overdependence on the idiosyncrasies of the dataset the model was developed on, which is evidenced by the fact that it seemed to predict well in that sample. Inevitably, this issue is a byproduct of sample size limitations.

6.2 Clinical Relevance/Applications

6.2.1 Generalizability

Due to the fact that this analysis was based on a small sample with a low number of cases, the generalizability of these results are limited. As reported in section 5.3.2, the predictive accuracy of this model is strong in the sample it was created in, but is compromised in the bootstrapped samples and should be applied with caution as a result.

This model is most appropriate for prospective use at the London Intercommunity Health Centre's prenatal clinic, and secondarily in clinics that serve a population with similar demographic characteristics and immigration patterns. Further, the application of this model is dependent on the use of the forms used in this analysis, or the collection of comparable information. Thus, clinics that have switched to an electronic medical record system may not have access to the same information.

6.3 Implications for Prevention

The ability to calculate the risk of experiencing a short interpregnancy interval for individual patients is highly useful from a public health perspective. There are a number of simple actions that can be taken to avert the negative outcomes associated with insufficient birth spacing that can be offered once a patient is identified as being high risk. In many cases, knowledge of the risk of adverse health outcomes associated with becoming pregnant within six months of giving birth alone may act as a preventative measure.

6.3.1 Family Planning and Access to Birth Control

An obvious way to avert the risks associated with short interpregnancy intervals is to ensure that high-risk patients have access to family planning counselling and contraception if it is of interest to them. Beyond providing basic access to services, an effective intervention would acknowledge that the contraceptive priorities of women who have previously given birth are different from those who have not, and the method of birth control they were previously using may no longer be desirable.[75] Among women studied in Atlanta, Georgia, women who were post-partum largely agreed that the ideal method of birth control would be reliable, effective, and reversible, and prioritized concerns about safety during breastfeeding.[75]

According to Edouard, family planning services aimed at underserved populations are most effective when they focus on informed choice, access to services, and lack of prejudice,[74] and should be cognizant of the fact that that over a third of women who experience unplanned pregnancies express a general dissatisfaction with their prior method of birth control.[75]

6.3.2 Folate Supplementation

For those who are choosing to conceive shortly after birth, a simple way to diffuse the risk associated with short interpregnancy intervals is to offer high-risk mothers additional folate supplementation at birth to reduce post-natal deficiency. The use of folate supplementation has been shown to be effective in mitigating the effect of short interpregnancy intervals on several outcomes, including low birthweight. Early folate use accompanying a short interpregnancy interval is associated with a decrease in birthweight of just 5.9 grams (SD +/-33.6 grams) compared to moderate interpregnancy intervals, while the late use of folate is associated with a decrease of 33.5 grams (SD +/-35.6 grams), and a decrease of 165.2 grams (SD +/- 39.6 grams) is associated with no folate supplementation.

Both access to family planning services and contraception, and early folate supplementation, are interventions that are early to implement and prioritize the autonomy of the patient.

6.4 Knowledge Transfer

An important part of the aim of this project is to ensure that the results are useful to the LIHC prenatal clinic. In order to ensure they have easy access to results, in addition to providing a copy of this text, a plain language summary has been developed. This summary is suitable for clinicians, administrators and patients. Additionally, the clinic has been involved in providing input on the format of the clinical tool in order to ensure it is as accessible and useful as possible.

6.5 Strengths

The greatest strength of this project is the ease with which results can be applied in a clinical setting. This study was designed to meet a clinic-identified need, and, if successful,

would do so with minimal burden on the clinic. This is because the data used was already collected in regular practice, and the nomogram can be used to calculate an individual's risk with little effort.

Another strength of this study stems from the use of clinical data. The use of information from forms mandated by the Ontario government makes it possible to apply the model in other clinical settings, therefore increasing generalizability.

6.6 Limitations

6.6.1 Sample Size

The most significant limitation of this study is the small sample size. Upon applying for approval from the Health Sciences Research Ethics Board at the University of Western Ontario, a formal sample size calculation was completed based on estimates of both the number of patients served per year by clinicians and the number of patients that would have experienced a previous birth, thus qualifying them for participation in this project. Unfortunately, the London Intercommunity Health Centre serves a limited number of patients, and far fewer than expected had experienced a previous birth. Thus, fewer patient files were available for inclusion than expected. We could not determine how many patients had experienced a previous live or still birth in advance because paper charts are still being used. Further, because this study was completed in its entirety in under 15 months, pilot testing could not be completed to determine the number of patients that would qualify for inclusion.

The effects of the sample size used in this analysis are far-reaching. First, interpretation of the results of this analysis, particularly odds ratios, is compromised by large confidence intervals. Second, despite best attempts to avoiding overfitting, it is likely that the results are bound too

closely to the idiosyncrasies of this dataset. A larger sample is needed to enhance the effectiveness of this model.

6.6.2 Use of Data Not Intended for Research

Another limitation of this study is the use of previously collected data that was not intended for research purposes. This inhibited our ability to explore a broader range of potential predictors based on existing literature and intuition. Further, the use of non-research data removed the ability to attempt to standardize the way questions were asked to patients, and the level of detail.

An additional limitation that arises from the use of this data source is that the utility of the model may be compromised if the provincially mandated forms are changed, or if this or other clinics switch to an electronic medical record system that does not include the same questions.

6.6.3 Temporality

This study is also limited by the fact that charted data were collected at first prenatal visit for the current pregnancy, that is once the birth-to-conception interval had already taken place. This is problematic because several of the factors may change from previous birth to current conception. Since the purpose of the project is to predict forward, some of the variables used in this analysis may not reflect their status at the desired time point.

6.7 Future Steps

In order to assess the utility of routinely collected clinical data in predicting short interpregnancy intervals, this model should be re-run using the same analysis techniques in a larger sample. This could be done quite simply if investigators had access to a larger patient

population, and electronic medical records. Further, it would be helpful to have more detailed information on mode of index birth,[76] breastfeeding status, and contraceptive use among patients.

In future models, both internal and external validation should occur by measuring the predictive accuracy prospectively in the population it was created in, and in other populations. If successful, this could be a highly useful tool in preventing negative health outcomes associated with short interpregnancy intervals, especially in underserved populations.

Finally, in order to gain a better understanding of why the variables identified in this study are important predictors of short interpregnancy intervals, and to better understand the reasons why women become pregnant again within six months of giving birth, a qualitative study should be conducted.

6.8 Conclusion

From its inception, a key aim of this project was to minimize the burden on the LIHC prenatal clinic while maximizing the utility of results. This aim is both the project's greatest strength and greatest weakness, as it limited the data available and sample size, but ensured the results can be applied in a clinical setting. Despite challenges, results may be applied cautiously in the London Intercommunity Health Centre prenatal clinic, and perhaps more broadly with additional testing.

Literature Cited

1. London Intercommunity Health Centre. London Intercommunity Health Centre: Welcome. Accessed on April 12, 2009. URL: http://www.lihc.on.ca/

2. Gold R, Connell FA, Heagerty P, Bezruchka S, Davis R, Cawthon ML. Income inequality and pregnancy spacing. Soc Sci Med 2004;59(6):1117-26.

3. Conde-Agudelo A, Rosas-Bermudez A, Kafury-Goeta AC. Birth spacing and risk of adverse perinatal outcomes: a meta-analysis. JAMA 2006;295(15):1809-23.

4. Conde-Agudelo A, Rosas-Bermudez A, Kafury-Goeta AC. Effects of birth spacing on maternal health: a systematic review. Am J Obstet Gynecol 2007;196(4):297-308.

5. Rahim A, Ram B. Emerging patterns of child-spacing in Canada. J Biosoc Sci 1993;25(2):155-67.

6. Statistics Canada. Births: 2006. Accessed on April 22, 2009. URL: http://www.statcan.gc.ca/pub/84f0210x/84f0210x2006000-eng.pdf.

7. Lesthaeghe R, & Moors, G. Recent trends in fertility and household formation in the industrialized world. Review of Population and Social Policy 2000;9.

8. Tudiver S. Changing fertility patterns: trends and implications. Health policy research. Vol. 10 Health Canada, 2005.

9. Tudiver S. Changing Fertility Patterns: Trends and Implications. In: Health Policy Research, ed. Vol. 10, 2005.

10. Hyde JSD, J.D.; Plant, E.A.; Byrd, J. M. Sexuality during pregnancy and the year postpartum. J Sex Research 1996;33(2):143-151.

11. Dixon M, Booth N, Powell R. Sex and relationships following childbirth: a first report from general practice of 131 couples. Br J Gen Pract 2000;50(452):223-4.

12. Barrett G, Pendry E, Peacock J, Victor C, Thakar R, Manyonda I. Women's sexual health after childbirth. BJOG 2000;107(2):186-95.

13. Howie PW, McNeilly AS, Houston MJ, Cook A, Boyle H. Fertility after childbirth: post-partum ovulation and menstruation in bottle and breast feeding mothers. Clin Endocrinol (Oxf) 1982;17(4):323-32.

14. Norris S. In brief: reproductive infertility: prevalence, causes, trends and treatments. In: Parliamentary Research Branch Library of Parliament, ed. Ottawa, ON, 2001.

15. King J. Contraception and lactation. J Midwifery Womens Health 2007;52(6):614-20.

16. Palda VA, Guise JM, Wathen CN. Interventions to promote breast-feeding: applying the evidence in clinical practice. CMAJ 2004;170(6):976-8.

17. Hiller JE, Griffith E, Jenner F. Education for contraceptive use by women after childbirth. Cochrane Database Syst Rev 2002(3):CD001863.

18. Glasier AF, Logan J, McGlew TJ. Who gives advice about postpartum contraception? Contraception 1996;53(4):217-20.

19. Radecki SE, Beckman LJ. Contraceptive risk-taking in a medically-underserved, low-income population. Women & Health 1994;21(1):1-15.

20. Srikanthan A, Reid RL. Religious and cultural influences on contraception. J Obstet Gynaecol Can 2008;30(2):129-37.

21. Kramer MR, Hogue CJ, Gaydos LM. Noncontracepting behavior in women at risk for unintended pregnancy: what's religion got to do with it? Ann Epidemiol 2007;17(5):327-34.

22. Statistics Canada. Pregnancy Outcomes: 2005. Accessed April 1, 2009. URL: http://www.statcan.gc.ca/pub/82-224-x/82-224-x2005000-eng.pdf

23. Henshaw SK. Unintended pregnancy in the United States. Fam Plann Perspect 1998;30(1):24-9, 46.

24. Klebanoff MA. Short interpregnancy interval and the risk of low birthweight. Am J Public Health 1988;78(6):667-70.

25. van Eijsden MS, Luc JM; van der Wal, Marcel F; Bonsel, Gouke J. Association between short interpregnancy intervals and term birth weight: the role of folate depletion. Am J Clin Nutr 2008;88.

26. Smits LJ, Essed GG. Short interpregnancy intervals and unfavourable pregnancy outcome: role of folate depletion. Lancet 2001;358(9298):2074-7.

27. King JC. The risk of maternal nutritional depletion and poor outcomes increases in early or closely spaced pregnancies. J Nutr 2003;133(5 Suppl 2):1732S-1736S.

28. Smits L, Zielhuis G, Jongbloet P, Bouchard G. The association of birth interval, maternal age and season of birth with the fertility of daughters: a retrospective cohort study based on family reconstitutions from nineteenth and early twentieth century Quebec. Paediatr Perinat Epidemiol 1999;13(4):408-20.

29. Khoshnood B, Lee KS, Wall S, Hsieh HL, Mittendorf R. Short interpregnancy intervals and the risk of adverse birth outcomes among five racial/ethnic groups in the United States. Am J Epidemiol 1998;148(8):798-805.

30. Tamura T, Picciano MF. Folate and human reproduction. Am J Clin Nutr 2006;83(5):993-1016.

31. Scholl TO, Johnson WG. Folic acid: influence on the outcome of pregnancy. Am J Clin Nutr 2000;71(5 Suppl):1295S-303S.

32. Bruinse HWavdB, H. Changes of some vitamin levels during and after normal pregnancy. Eur J Ob Gyn Reprod Biol 1995;61.

33. Scholl TO, Hediger ML, Schall JI, Khoo CS, Fischer RL. Dietary and serum folate: their influence on the outcome of pregnancy. Am J Clin Nutr 1996;63(4):520-5.

34. Joseph KS, Kramer MS, Marcoux S, Ohlsson A, Wen SW, Allen A, Platt R. Determinants of preterm birth rates in Canada from 1981 through 1983 and from 1992 through 1994. N Engl J Med 1998;339(20):1434-9.

35. Canadian Institute for Health Information. Too Early, Too Small: A Profile of Small Babies Across Canada. Ottawa, ON, 2009.

36. Johnston RB, Jr., Williams MA, Hogue CJ, Mattison DR. Overview: new perspectives on the stubborn challenge of preterm birth. Paediatr Perinat Epidemiol 2001;15 Suppl 2:3-6.

37. Miller JE. Birth intervals and perinatal health: an investigation of three hypotheses. Fam Plann Perspect 1991;23(2):62-70.

38. Adams MM, Delaney KM, Stupp PW, McCarthy BJ, Rawlings JS. The relationship of interpregnancy interval to infant birthweight and length of gestation among low-risk women, Georgia. Paediatr Perinat Epidemiol 1997;11 Suppl 1:48-62.

39. Ekwo EE, Moawad A. The relationship of interpregnancy interval to the risk of preterm births to black and white women. Int J Epidemiol 1998;27(1):68-73.

40. Fuentes-Afflick E, Hessol NA. Interpregnancy interval and the risk of premature infants. Obstet Gynecol 2000;95(3):383-90.

41. Klerman LV, Cliver SP, Goldenberg RL. The impact of short interpregnancy intervals on pregnancy outcomes in a low-income population. Am J Public Health 1998;88(8):1182-5.

42. Rawlings JS, Rawlings VB, Read JA. Prevalence of low birth weight and preterm delivery in relation to the interval between pregnancies among white and black women. N Engl J Med 1995;332(2):69-74.

43. Smith GCSP, Jill P.; Dobbie, Richard. Interpregnancy interval and risk of preterm birth and neonatal death: retrospective cohort study. BMJ 2008;327(313).

44. Shults RA, Arndt V, Olshan AF, Martin CF, Royce RA. Effects of short interpregnancy intervals on small-for-gestational age and preterm births. Epidemiology 1999;10(3):250-4.

45. Basso O, Olsen J, Knudsen LB, Christensen K. Low birth weight and preterm birth after short interpregnancy intervals. Am J Obstet Gynecol 1998;178(2):259-63.

46. DeFranco EA, Stamilio DM, Boslaugh SE, Gross GA, Muglia LJ. A short interpregnancy interval is a risk factor for preterm birth and its recurrence. Am J Obstet Gynecol 2007;197(3):264 e1-6.

47. Hokken-Koelega AC, De Ridder MA, Lemmen RJ, Den Hartog H, De Muinck Keizer-Schrama SM, Drop SL. Children born small for gestational age: do they catch up? Pediatr Res 1995;38(2):267-71.

48. Statistics Canada. Deaths: 2006. Accessed on March 23, 2009. URL: http://www.statcan.gc.ca/pub/84f0211x/84f0211x2006000-eng.pdf.

49. Kallan JE. Reexamination of interpregnancy intervals and subsequent birth outcomes: evidence from U.S. linked birth/infant death records. Soc Biol 1997;44(3-4):205-12.

50. Stephansson O, Dickman PW, Cnattingius S. The influence of interpregnancy interval on the subsequent risk of stillbirth and early neonatal death. Obstet Gynecol 2003;102(1):101-8.

51. Roberts JM. Preeclampsia: what we know and what we do not know. Semin Perinatol 2000;24(1):24-8.

52. Healthy Ontario. Conditions: Preeclampsia. Accessed June 1, 2009. URL: http://www.healthyontario.com/ConditionDetails.aspx?disease_id=107.

53. Trogstad LI, Eskild A, Magnus P, Samuelsen SO, Nesheim BI. Changing paternity and time since last pregnancy; the impact on pre-eclampsia risk. A study of 547 238 women with and without previous pre-eclampsia. Int J Epidemiol 2001;30(6):1317-22.

54. Basso O, Christensen K, Olsen J. Higher risk of pre-eclampsia after change of partner. An effect of longer interpregnancy intervals? Epidemiology 2001;12(6):624-9.

55. Conde-Agudelo A, Belizan JM. Maternal morbidity and mortality associated with interpregnancy interval: cross sectional study. BMJ 2000;321(7271):1255-9.

56. Skjaerven R, Wilcox AJ, Lie RT. The interval between pregnancies and the risk of preeclampsia. N Engl J Med 2002;346(1):33-8.

57. Khan KS, Wojdyla D, Say L, Gulmezoglu AM, Van Look PF. WHO analysis of causes of maternal death: a systematic review. Lancet 2006;367(9516):1066-74.

58. Public Health Agency of Canada. Report on Maternal Mortality in Canada. 1998. Accessed on June 1, 2009. URL: http://www.phac-aspc.gc.ca/rhs-ssg/matmort-eng.php.

59. Pinto-Martin JA, Cnaan A, Zhao H. Short interpregnancy interval and the risk of disabling cerebral palsy in a low birth weight population. J Pediatr 1998;132(5):818-21.

60. Smits LP, Carsten; Mortensen, Preben; van Os, Jim. Association between short birth intervals and schizophrenia in the offspring. Schiz Res 2004;70.

61. Hayes H, Luchok K, Martin AB, McKeown RE, Evans A. Short birth intervals and the risk of school unreadiness among a Medicaid population in South Carolina. Child Care Health Dev 2006;32(4):423-30.

62. Kaharuza FM, Sabroe S, Basso O. Choice and chance: determinants of short interpregnancy intervals in Denmark. Acta Obstet Gynecol Scand 2001;80(6):532-8.

63. Gold R, Connell FA, Heagerty P, Cummings P, Bezruchka S, Davis R, Cawthon ML. Predicting time to subsequent pregnancy. Matern Child Health J 2005;9(3):219-28.

64. Harrell FE, Jr., Lee KL, Mark DB. Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. Stat Med 1996;15(4):361-87.

65. Steyerberg EW, Eijkemans MJ, Harrell FE, Jr., Habbema JD. Prognostic modeling with logistic regression analysis: in search of a sensible strategy in small data sets. Med Decis Making 2001;21(1):45-56.

66. Harrell FE, Jr. . Regression Modeling Strategies: With Applications to Linear Models, Logistic Regression and Survival Analysis. Springer Series in Statistics. Nashville: Springer, 2001.

67. Pigott TD. A review of methods for missing data. Educational Research and Evaluation 2001;7(4):353-383.

68. Schafer JL, Graham JW. Missing data: our view of the state of the art. Psychol Methods 2002;7(2):147-77.

69. Hosmer DWL, S. Applied Logistic Regression. New York: Wiley, 2004.

70. Nabukera SK, Wingate MS, Salihu HM, Owen J, Swaminathan S, Alexander GR, Kirby RS. Pregnancy spacing among women delaying initiation of childbearing. Arch Gynecol Obstet 2009;279(5):677-84.

71. Citizenship and Immigration Canada. Resettlement from outside Canada: Arriving - health care. Accessed June 16, 2009. URL: http://www.cic.gc.ca/english/refugees/outside/arriving-healthcare.asp.

72. Kealy L. Women refugees lack access to reproductive health services. Popul Today 1999;27(1):1-2.

73. Goodyear L, McGinn T. Emergency contraception among refugees and the displaced. J Am Med Womens Assoc 1998;53(5 Suppl 2):266-70.

74. Edouard L. The right to contraception and the wrongs of restrivtive services. Int J Gynecol Obstet 2009;12(1).

75. Cwiak C, Gellasch T, Zieman M. Peripartum contraceptive attitudes and practices. Contraception 2004;70(5):383-6.

76. Eijsink JJ, van der Leeuw-Harmsen L, van der Linden PJ. Pregnancy after Caesarean section: fewer or later? Hum Reprod 2008;23(3):543-7.

Appendices

Appendix A: Approval from UWO Health Science Research Ethics Board

Office of Research Ethics

The University of Western Ontario
Room 4180 Support Services Building, London, ON, Canada N6A 5C1
Telephone: (519) 661-3036 Fax: (519) 850-2466 Email: ethics@uwo.ca
Website: www.uwo.ca/research/ethics

Use of Human Subjects - Ethics Approval Notice

Principal Investigator: Dr. G. Bauer
Review Number: 15447E **Review Level:** Expedited
Review Date: September 04, 2008
Protocol Title: Predicting Interpregnancy Intervals in Women from Underserved Populations in London, Ontario
Department and Institution: Epidemiology & Biostatistics, University of Western Ontario
Sponsor:
Ethics Approval Date: October 01, 2008 **Expiry Date:** September 30, 2009
Documents Reviewed and Approved: UWO Protocol
Documents Received for Information:

This is to notify you that The University of Western Ontario Research Ethics Board for Health Sciences Research Involving Human Subjects (HSREB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the Health Canada/ICH Good Clinical Practice Practices: Consolidated Guidelines; and the applicable laws and regulations of Ontario has reviewed and granted approval to the above referenced study on the approval date noted above. The membership of this REB also complies with the membership requirements for REB's as defined in Division 5 of the Food and Drug Regulations.

The ethics approval for this study shall remain valid until the expiry date noted above assuming timely and acceptable responses to the HSREB's periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the UWO Updated Approval Request Form.

During the course of the research, no deviations from, or changes to, the protocol or consent form may be initiated without prior written approval from the HSREB except when necessary to eliminate immediate hazards to the subject or when the change(s) involve only logistical or administrative aspects of the study (e.g. change of monitor, telephone number). Expedited review of minor change(s) in ongoing studies will be considered. Subjects must receive a copy of the signed information/consent documentation.

Investigators must promptly also report to the HSREB:

a) changes increasing the risk to the participant(s) and/or affecting significantly the conduct of the study;
b) all adverse and unexpected experiences or events that are both serious and unexpected;
c) new information that may adversely affect the safety of the subjects or the conduct of the study.

If these changes/adverse events require a change to the information/consent documentation, and/or recruitment advertisement, the newly revised information/consent documentation, and/or advertisement, must be submitted to this office for approval.

Members of the HSREB who are named as investigators in research studies, or declare a conflict of interest, do not participate in discussion related to, nor vote on, such studies when they are presented to the HSREB.

[redacted]

Chair of HSREB: Dr. Joseph Gilbert

Ethics Officer to Contact for Further Information			
☐ Janice Sutherland [redacted]	☐ Elizabeth Wambolt [redacted]	☐ Grace Kelly [redacted]	☑ Denise Grafton [redacted]

This is an official document. Please retain the original in your files.

cc: ORE File

Appendix B: Antenatal Record 1

Ontario Medical Association — *In conjunction with the* — Ontario Ministry of Health and Long-Term Care

Antenatal Record 1

Patient's Last Name	Patient's First Name		
Address – number, street name		Apt/Suite/Unit	
City/Town	Province	Postal Code	
Telephone - Home	Telephone - Work	Language	
Date of birth	Age	Occupation	Educational level
OHIP No.	Patient File No.	Marital status	

Partner's Last Name	Partner's First Name	
Partner's Occupation	Partner's Educational level	Age

Ethnic or Racial backgrounds: Mother / Father

Birth attendant	Newborn care	Family Physician

Allergies or Sensitivities (describe reaction details)

Medications/Herbals

Pregnancy Summary

LMP	Certain Yes ☐ No ☐	EDB (by dates)	**Final EDB**
Cycle q ____	Regular Yes ☐ No ☐		Dating Method
Contraceptive type	Last used		☐ Dates
			☐ T_1 US
			☐ T_2 US
			☐ ART (e.g. IVF)

Gravida	Term	Premature	Abortuses	Living

Obstetrical History

No.	Year	Sex M/F	Gest. age (weeks)	Birth weight	Length of labour	Place of birth	Type of delivery	Comments regarding pregnancy and birth

Medical History and Physical Exam (provide details in comments)

Current Pregnancy

1. Bleeding Y / N
2. Nausea, vomiting Y / N
3. Smoking ___cig/day Y / N
4. Alcohol, street drugs Y / N
5. Occup/Environ. risks Y / N
6. Dietary restrictions Y / N
7. Calcium adequate Y / N
8. Preconceptual folate Y / N

Medical History

9. Hypertension Y / N
10. Endocrine Y / N
11. Urinary tract Y / N
12. Cardiac/Pulmonary Y / N
13. Liver, hepatitis, GI Y / N
14. Gynaecology/ Breast Y / N
15. Hem./Immunology Y / N
16. Surgery Y / N
17. Blood transfusion Y / N
18. Anaesthetic compl. Y / N
19. Psychiatric Y / N
20. Epilepsy/ Neurological Y / N
21. Other Y / N

Genetic History

22. At risk population Y / N
(e.g.: Ashkenazi, consanguinity, CF, sickle cell, Tay Sachs, thalassemia)

Family history of:

23. Developmental delay Y / N
24. Congenital anomalies Y / N
25. Chromosomal disorders Y / N
26. Genetic disorders Y / N

Infectious Disease

27. Varicella susceptible Y / N
28. STDs / HSV / BV Y / N
29. Tuberculosis risk Y / N
30. Other Y / N

Psychosocial

31. Poor social support Y / N
32. Relationship problems Y / N
33. Emotional/Depression Y / N
34. Substance abuse Y / N
35. Family violence Y / N
36. Parenting concerns Y / N
37. Relig. / Cultural issues Y / N

Family History

38. At risk population Y / N
(e.g.: DM, DVT/PE, PIH/HT, postpartum depression, thyroid)

Physical Examination

Ht._____ Wt._____

BMI_____ BP _____

39. Thyroid N / Abn
40. Chest N / Abn
41. Breasts N / Abn
42. Cardiovascular N / Abn
43. Abdomen N / Abn
44. Varicosities / Extrm. N / Abn
45. External genitalia N / Abn
46. Cervix, vagina N / Abn
47. Uterus N / Abn
48. Size: _____ weeks
49. Adnexae N / Abn
50. Other N / Abn

Initial Laboratory Investigations

Test	Result	Test	Result
Hb		HIV	
MCV		☐ Counseled and test declined	
ABO		Last Pap	
Rh			
Antibody Screen		GC/Chlamydia	
Rubella immune		Urine C&S	
HBsAg			
VDRL			
Sickle Cell			

Prenatal Genetic Investigations	Result
a) All ages-MSS, IPS, FTS	
b) Age ≥ 35 at EDB-CVS/amnio	
c) If a or b declined, or twins, then MSAFP	
d) Counseled and test declined, or too late	☐

Comments

Signature	Date	Signature	Date

4293-64 (05/03) Canary – Mother's chart – forward to hospital Pink – Attendant's copy White – infant's chart 7530-5624

Appendix C: London Intercommunity Health Centre Client Intake Form

The information below will be used for statistics purposes only and is strictly confidential, in compliance with Provincial Privacy Legislation.

Country of Origin: _____ Year of arrival in Canada: _____

Cultural Background (e.g. religion, race, parent's/ancestors' country of origin): _____

Describe who lives with you:

☐ Couple with child(ren) ☐ Couple without child ☐ Extended Family

☐ Sole Member (Male/Female) ☐ Unrelated Housemates ☐ Siblings

☐ Single parent family (mother head) ☐ Single parent family (father head)

☐ Grandparents with grandchild(ren) ☐ Other _____

Education:

☐ Elementary ☐ High School ☐ University ☐ College ☐ No Formal Education

Household Income:

☐ 0-14,999 ☐ 15,000-19,999 ☐ 20,000-24,999 ☐ 24,999-29,999 ☐ 30,000-34,000

☐ 35,000-39,999 ☐ 40,000-59,999 ☐ over 50,000

Number of people supported by this income : _____

Appendix D: Continent and Country of Origin: Full Sample

Continent of Origin (n=187)		
North America	93	49.73
South America	16	8.56
Asia	37	19.79
Africa	28	14.97
Europe	13	6.95
North America (n=93)		
Canada	87	46.03
Jamaica	1	0.53
Mexico	2	1.06
St. Vincent	1	0.53
United States	2	1.06
South America (n=16)		
El Salvador	9	56.25
Guatemala	2	12.50
Honduras	1	6.25
Nicaragua	3	18.75
Venezuela	1	6.25
Asia (n=37)		
Afghanistan	4	10.81
Bangladesh	2	5.41
Burma	2	5.41
Cambodia	12	32.43
Egypt	1	2.70
Iran	3	8.11
Iraq	5	13.51
Kuwait	1	2.70
Lebanon	1	2.70
Pakistan	3	8.11
Syria	2	5.41
Yemen	1	2.70
Africa (n=28)		
Angola	2	7.14
Burundi	1	3.75
Republic of Congo	2	7.14
Eritrea	2	7.14
Kenya	1	3.75
Rwanda	1	3.75
Somalia	2	7.14
Sudan	12	42.86
Uganda	2	7.14
Zaire	1	3.75

Zimbabwe	2	7.14
Europe (n=13)		
Albania	4	30.77
Bosnia	2	15.38
Croatia	1	7.69
France	1	7.69
Kosovo	1	7.69
Portugal	1	7.69
Romania	1	7.69
Russia	1	7.69
(Former) Yugoslavia	1	7.69

Appendix E: Continent and Country of Origin: Cases Only

Continent of Origin (n=20)		
North America	11	55.00
South America	1	5.00
Asia	4	20.00
Africa	4	20.00
Europe	0	0
Country (n=20)		
Canada	10	50.00
Afghanistan	1	5.00
Cambodia	1	5.00
El Salvador	1	5.00
Iraq	1	5.00
Mexico	1	5.00
Syria	1	5.00
Somalia	1	5.00
Sudan	3	15.00